Drug and Cosmetic Industry

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"The only trouble is my thumb gets sore."

Keeping Posted

Tetracycline Patent Suits Settled

The tetracycline patent suits between Chas. Pfizer & Co., and Bristol Laboratories, The Upjohn Company, and E. R. Squibb & Sons Division, Olin Mathieson Chemical Corporation have been resolved. A settlement was reached and all suits were withdrawn on March 28. These suits date back to January 11, 1955, the day on which a basic patent on tetracycline was issued to Chas. Pfizer & Co.

Under the terms of the settlement, Bristol, Upjohn and Squibb were granted non-exclusive, royalty-bearing licenses for the use and sale of tetracycline under the product claims of the Pfizer patent, effective from the day the Pfizer patent was issued. In addition, Bristol was licensed to manufacture tetracycline. Pfizer and Bristol also exchanged options to obtain licenses under their United States and foreign patent rights relating to processes for the production of tetracycline. All four companies will continue to sell the antibiotic under their respective brand names in the United States and elsewhere.

This settlement means that Bristol, Upjohn, and Squibb have agreed to recognize the Pfizer patent as valid in return for licenses to continue to sell (and Bristol also to manufacture) tetracycline. Also these companies have agreed to pay back royalties from January 11, 1955, as well as royalties from now on.

Kordolin Claims Banned

In an opinion by Commissioner Lowell B. Mason, the Federal Trade Commission adopted a hearing examiner's findings that Kordolin Tablets give only partial and temporary relief from minor aches and pains caused by arthritis and rheumatism. The examiner had ordered Kordol Corporation of America, New York, to stop claiming that the tablets 1, are a new or amazing discovery, 2, are more effective as a pain reliever than aspirin, or 3, will afford any relief of severe aches, pains and discomfort of the ailments or have any therapeutic effect on their underlying causes, symptoms or manifestations except temporary and partial relief of the minor aches and pains.

On appeal by counsel supporting the complaint, the Commission modified the order by dropping "underlying causes." Commissioner Mason approved counsel's contention that the implication of the examiner's order is that Kordolin's relief of minor aches and pains may have an effect on underlying causes. "On the contrary," Commissioner Mason said, "we are of the opinion, and so find, that the evidence is undisputed that Kordolin will have no effect on 'underlying causes.'"

More Lilly Salk Vaccine

Eli Lilly and Company is greatly increasing the harvesting and testing of polio vaccine in an effort to make an extra 20 million doses available by June 30. Harvesting has been stepped up 50 per cent to a production rate of 6,800,000 cc. a month. The company hopes to submit a total of 60 million cc. to the National Institutes of Health during the first six months of this year. Originally the company's goal was 40 million cc. by June 30. To reach the 60 million total, Lilly has enlarged its testing activities to process a large backlog of vaccine which has been harvested but not tested.

However, a company official said: "it should be emphasized that this is a goal yet to be accomplished. There are many uncertainties in this business. While we are optimistic about reaching the goal, we should all realize that the bird is not yet in the hand but is still in the bush."

Fluoride Dentifrices

Sodium Fluoride Dentifrices, formerly restricted to sales on prescriptions only, are now allowed to be sold over the counter if they meet the following requirements contained in the Food and Drug Administration order:

1. The sodium fluoride is prepared, with other components, in a dosage form suitable for household use

Take Dreyer Spray-dried Flavors

All the fine, full flavors your fine foods need are spray-dried for you now by Dreyer.

Dreyer makes them by today's most modern methods, using Dreyer's expert skills to safeguard them. They are very high quality flavors, in a wide, varied range. You can most profitably use them to improve the taste of popular products, and for desired, quick flavor changes.

On your business letterhead request free samples that show you their long-lasting excellence. It is time you tried Dreyer spray-dried Flavors.

Dreyer Spray-Dried Flavors include:

Apple, Banana, Cherry, Wild Cherry, Grape, Peach, Pineapple, Raspberry, Root Beer, Strawberry, Oil Lemon, Oil Lemon-Lime, Oil Lime, Oil Orange

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P. R. Dreyer Inc.
Serving You Since 1920

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Complete stocks carried in Chicago

Dreyer

as a dentifrice powder, and containing no drug limited to prescription sale under the provisions of section 503 (b) (1) of the act.

2. The sodium fluoride and all other components of the preparation meet their professed standards of identity, strength, quality, and purity.

3. If the preparation is a new drug, an application pursuant to section 505 (b) of the act is effective for it.

4. The preparation contains not more than 5 milligrams of sodium fluoride per gram and is packaged to contain not more than 300 milligrams of sodium fluoride per retail package.

5. The preparation is labeled with adequate directions for use only as a dentifrice by adults and children six years of age and over, and includes instructions to rinse the mouth thoroughly after brushing the teeth.

6. The labeling bears, in juxtaposition with the directions for use, clear warning statements against:

a. Use by children under six years of age.

b. Use if the water supply contains fluoride, except as directed by a dentist.

F.T.C. Cites Revlon

Revlon Products Corporation has been charged by the Federal Trade Commission with unfair discrimination among customers in the granting of sales promotion aid. Revlon is charged with violation of the Robinson-Patman to the Clayton Act because of failure to make available to competing customers promotional allowances and services on "proportionately equal terms." It is charged that of 118 customers in the Washington, D.C. trade area about 26 received services or allowances and about 92 did not. Of the 26, some received allowances of as much as 22.5 per cent, while others received as little as 3.3 per cent. The per cent of the customers' advertising cost defrayed by Revlon is said to range from 69.4 per cent to 100 per cent. It is charged further that some but not all of the 26 were required to enter into promotional contracts and file reports. Similar practices are said to have been carried on in such major cities as Baltimore, Cleveland, Chicago, and San Francisco.

The Commission states that this is the fifth case brought as the result of its investigation to determine whether companies are complying with the Trade Practice Rules for the Cosmetic and Toilet Preparations Industry. The four other complaints were filed last November. Revlon's payments to customers are said to cover such items as cooperative advertising, demonstrator services, and push money.

F.T.C. Cites United-Whelen

The Federal Trade Commission has brought action against United-Cigar Whelen Stores Corporation and four suppliers who paid United-Whelen a total of $38,000 in 1954 for participation in television shows sponsored by United-Whelen. The suppliers and their principal products are: Bymart-Tintair, Inc., Tintair, Touch-Up, and Lightening Change (Hair Tints); Serutan Company, Serutan and R.D.X.; Johnson & Johnson, surgical dressings, first aid kits, and baby products; Anahist Company, Anahist Tablets and Hist-O-Plus.

The suppliers are charged with giving special allowances to United-Whelen in return for advertising on the T.V. shows without making such allowances available to competing customers on "proportionately equal terms."

United-Whelen is charged with inducing or receiving these allowances which it "knew or should have known" were not being offered to its competitors; this being an unfair method of competition in violation of the Federal Trade Commission Act. The complaint against United-Whelen also includes Product Advertising Corporation, its wholly owned subsidiary and advertising agency. The complaint alleges the firms negotiated contracts with suppliers to participate in the programs, Whelen's Playhouse, Whelen's Film Playhouse, or Whelen's Cavalcade of Stars. In return for inclusion in the commercials each supplier contributed to the cost of the program in which its products were featured. The complaint states that in 1954, 57 suppliers entered into this plan and paid an aggregate of $363,000 to United-Whelen. Most of the suppliers, including the four cited, failed to give proportionately equal treatment to other customers, according to the Commission.

Elmo-F.T.C. Case Settled

A consent order has been issued against Elmo, Inc., by the Federal Trade Commission prohibiting the Philadelphia firm from discriminating among its customers in granting of promotional aid. The agreement is for settlement purposes only and does not constitute an admission by the firm that it has violated the law. The Elmo case was one of the four brought last November by the Commission after its investigation to determine whether manufacturers were complying with the Trade Practice Rules for the Cosmetic and Toilet Preparations Industry.

Massachusetts Fair Trade Upheld

The Supreme Judicial Court of Massachusetts last month unanimously upheld the constitutionality of that state's fair trade law and of the McGuire Act in the case of General Electric Company v. Kimball Jewelers. This was the Massachusetts high court's first decision on fair trade. Massachusetts is the eighteenth state in which the high courts have upheld the constitutionality of fair trade with respect to state laws and the Federal enabling act, the McGuire Act.

SFK Gets Spansule Patent

Smith, Kline & French Laboratories has been granted their first patent in the new sustained release field of medicine which SKF introduced under the trademark Spansule. U. S. Patent No. 2,738,303 has been issued specifically to cover SKF's Benzadrine (amphetamine sulfate SKF) Spansule capsules, Dexamyl (dextro-amphetamine sulfate-amobarbital SKF) Spansule capsules, and Dexedrine (dextro-amphetamine sulfate SKF Spansule capsules. Patents are pending on the

Why you should use 'ROCHE' THIAMINE

HYDROCHLORIDE AND MONONITRATE

(vitamin B_1)

Here are ten persuasive reasons why 'Roche' thiamine should be your choice for pharmaceutical manufacturing

1. **U. S. P.** Both 'Roche' thiamine hydrochloride and mononitrate equal or exceed U. S. P. specifications.

2. **TWO TYPES.** Roche has *two types* of thiamine hydrochloride available for you:

   Regular—*for tablets, capsules, dry and liquid nutritive supplements and multivitamin preparations.*

   Ampul—*specially prepared for use in manufacturing parenteral solutions.*

3. **SPECIAL PROBLEMS.** Roche has thiamine mononitrate to help you meet unusual stability problems which can occur in dry cereal or pharmaceutical products. Also it may have advantages in certain pharmaceutical products where the pH range is above the safe level for the hydrochloride.

4. **STEADY SUPPLY.** Because Roche makes *quality* thiamine by the tons, you can be sure of a steady, *quality* supply.

5. **RESEARCH.** Continuing world-wide research brings you the latest developments in vitamin knowledge.

6. **PRODUCTION CONTROL.** Scientific production control assures you of consistent, highest quality.

7. **QUICK DELIVERY.** Every order receives prompt careful service from convenient points. Transportation at lowest rate allowed and prepaid to destination. Special routings at cost. And you *know* you can count on our promises.

8. **PACKAGING.** Packed in polyethylene bags in ½ and 1-kilo tamper-pruf metal containers and in fibre drums up to 20 kilos for the hydrochloride, 35 kilos for the mononitrate. Small quantities in amber S.C. bottles. *Ampul type* thiamine hydrochloride is sealed under inert gas in 100 gram S.C. bottles and in ½ and 1-kilo tamper-pruf metal containers.

9. **KNOW-HOW.** Roche know-how on vitamins can help you with solutions to compounding and packaging problems.

10. **SAMPLES** and technical assistance are yours on request. Ask your Roche salesman or write the Vitamin Division.

Make a note now... **CALL ROCHE FOR VITAMINS**

Vitamin Division • HOFFMANN-LA ROCHE INC. • Nutley 10, New Jersey

NUtley 2-5000

Pacific Coast distributor: **L. H. BUTCHER COMPANY, San Francisco • Los Angeles • Seattle • Portland • Salt Lake City**

In Canada: **Hoffmann-La Roche Ltd., 286 St. Paul Street, West; Montreal, Quebec**

firm's other Spansule capsule preparations and, in addition, a process patent has been applied for on the entire Spansule capsule line.

Restrictive Sales in N. J.

The fight over restrictive sales of drug preparations goes on in New Jersey. The Proprietary Association is centering its fight in this state in an attempt to have enacted legislation that will permit more free distribution of drug products. However, the New Jersey Pharmaceutical Association is fighting back and has submitted an alternate bill that would thwart the efforts of the Proprietary Association.

A key provision of the New Jersey Pharmaceutical Association's bill would:

Set up a three-member Commission comprising the president of the State Board of Pharmacy, the president of the State Board of Medical Examiners, and the State Health Commissioner, who would be empowered to determine which packaged drugs are habit-forming, and labeled with cautions requiring supervised sales, and liable to be destructive to human life when the full contents in which sold are taken at one time.

Another provision would:

Permit the unsupervised sales of certain popular packaged drugs and medicines such as Aspirin, Bufferin, Anacin, Alka Seltzer, Bisodol, Tums, Pepto-Bismol, if it does under the safeguard that the full contents of the package in which sold will not cause bodily injury if taken at one time, or that they are not labeled with such cautions or warnings as will limit their safe use.

It will be noted that the proposed commission would be composed of one pharmacist and two doctors, none of which would be likely to go out of their way to ease the restrictions surrounding the sale of drugs. Furthermore, the requirement that the entire contents if taken at one time not cause bodily harm, just about prohibits the sale of any of the so-called popular products with the possible exception of not more than three.

CIBS Award to Dr. Blank

Irvin H. Blank, Ph.D., of Harvard University Medical School is to be awarded the Fourth Annual CIBS Scientific Award for his paper, Mechanism of Agents for the Relief of Dry Skin, which was selected as the best paper given before the two scientific sessions of the Toilet Goods Association during 1955. The award consists of a scroll and a monetary prize of $250. It is designed "to stimulate more and original scientific investigation in the cosmetic industry."

Dr. Blank, associated with the dermatology departments at Harvard and Massachusetts General Hospital, will receive the award at the TGA Scientific Section meeting, May 17. CIBS president David J. Warner, of Fleuroma, Inc., will make the presentation. Dr. Samuel Zuckerman, of H. Kohnstamm & Company, chairman of the CIBS scientific committee, says that many people consider Dr. Blank's findings one of the most important contributions to cosmetic science in recent years.

Most of the products currently designed for the relief of dry skin are oil-based formulations, based on the assumption that skin's dryness is due to a loss of oils. Dr. Blank has shown that the condition known as dry skin is due to a loss of water from a layer called the stratum corneum. The oil-based formulations relieve the dry skin by forming a protective coating which prevents any further water loss from the stratum corneum. Industry observors feel that the knowledge of this mechanism will permit the formulation of even more effective skin-care preparations.

Dr. Blank's prize-winning paper was published in this magazine in June 1955, page 758.

T.G.A. Annual Meeting

The business program of the annual meeting of the Toilet Goods Association, to be held May 15, 16, 17, at the Waldorf-Astoria Hotel, New York, will deal chiefly with the problem of how the cosmetic and toilet goods industry can secure a larger part of the consumer's dollar during 1956, says Robert E. Schwartz, executive vice-president, Wildroot Company, and chairman of the T.G.A. Convention Program Committee. According to Mr. Schwartz, the coming meeting will focus more sharply on spots where cosmetic and toilet goods people may be missing the boat.

An innovation this year will be a session devoted to executive problems arising out of packaging and production. Changes in this area of the industry have been revolutionary and in the past only the big companies have been able to put them completely into practice. The result has been that small companies have been placed to some extent at a competitive disadvantage. Under the supervision of Ed Love, production manager for Bristol-Myers Company, an expert in the field of packaging and production, an entire session of the meeting will be devoted to efforts to minimize the small company's disadvantage. The importance of packaging design to sales and reduction of costs through automatic and semi-automatic equipment along with the latest advances in plastics and other packaging materials will be fully presented so that all members of the industry may take advantage of these developments.

A second session under the direction of Albert E. Ritchie, vice-president in charge of sales for the Wildroot Company, will cover management and selling problems in cooperation with the National Sales Executives of America. The idea behind this session, according to Mr. Ritchie, is "to find out how the stars do it." Other subjects to be covered in this session are the application of automation to small businesses and a discussion of profitable markets still untapped by larger companies.

John H. Breck Jr., executive vice-president of John H. Breck, Inc., will direct the session on advertising. His company is considered an important example of the work of a medium sized company in facing the fierce competition arising from the giants in the cosmetic and toilet goods field. With companies such as his own in mind, Mr. Breck will direct the advertising session generally toward helping the smaller manufacturer. "How to get into television without excessive costs," "How radio can be a better buy than before,"

* Geranidar

...when the cost of geranium goes up, the value of an excellent replacement is more important than ever... Geranidar is just such a replacement...

...the odor, value, character and stability of Geranidar have been time-tested for years.

Write on your letterhead for samples and suggestions.

SYNTOMATIC CORPORATION

114 East 32nd Street • New York 16, N. Y.

Cable Address: SYNTOMAT, N.Y.

*Reg. U.S. Pat. Office

"Why in this T.V. age, magazines and newspapers are more important than ever," will all be discussed in this advertising session.

The final day of the meeting will as usual be devoted to a meeting of the Scientific Section of the Association. These morning and afternoon sessions will be presided over by Dr. Dan Dahle, chairman of the section.

Papers to be given before the Scientific Section meeting are:

The Chemistry of Lauric Acid—Diethanolamine Condensation Products, by Harry Knoll, Geigy Chemical Corporation; Axillary Perspiration—Odors and Deodorization, by W. G. Fredell and R. R. Read, Lambert-Hudnut Division, Warner-Lambert Pharmaceutical Company; The Sphere of Research, by Paul G. Lauffer, The George W. Luft Company; The Physicochemical Characterization of Essential Oil Constituents and Their Derivatives by Modern Instrument Techniques, by Leo Levi and James L. Thomson, Food and Drug Laboratories, Department of National Health and Welfare, Ottawa, Canada, and James C. Evans and Harold Bernstein, Pure Chemistry Division, National Research Council, Ottawa; Problems in Dispensing Powders from Pressurized Containers, by Victor Di Giacomo, Givaudan-Delawanna, Inc.; Shampoos—A Practical Method of Evaluation, by W. G. Fredall and R. R. Read, Lambert-Hudnut Division, Warner-Lambert Pharmaceutical Company; Toxicity Studies on Monoethanolamine Thioglycolate Cold Waving Lotions by Ross Whitman and Martin G. Brookins, Rayette, Inc.; Azulene and Its Derivatives, by H. K. Thomas, Ph.D., and H. G. Gribou, Ph. D., Research Department, Dragoco.

Si-No Claims Stopped

Ethical Products, Inc., Detroit, has stipulated with the Federal Trade Commission to stop claiming that Si-No is a cure for sinusitis. The stipulation contains the following prohibitions for the product which is advertised as "hard-fighting capsules and effective Vitamin-Amino Acid Tablets:"

That Si-No is a remedy or cure for sinus ailments or has any value in preventing or treating these ailments except for temporary relief of minor sinus headaches and other sinus aches and pains;

That Si-No is a remedy, cure or competent treatment for, or will afford relief from, severe headaches or severe aches and pains;

That Si-No builds resistance against sinus attacks;

That Si-No No. 2 Pink Tablets, or the vitamins or amino acids contained in them, have any value in the prevention, relief or treatment of sinus ailments.

Hypertension Remedies

Almost simultaneously, two new and different chemicals have been announced as new drug products for control hypertension. Both are ganglionic blocking agents. One, announced by Sharp & Dohme, Division of Merck & Co., mecamylamine hydrochloride, trademarked Inversine. This is an entirely new compound synthesized in the Merck, Sharp & Dohme Research Laboratories, and found to be the best of dozens of compounds made and tested. The other, announced by Ciba Pharmaceutical Products, is chlorisondamine, trademarked Ecolid. This drug, which can be used along or in combination tranquilizing drugs such as reserpine, is said to be more effective, act faster, last longer, and be more free of side effects than products. Apparently the race is swift in this class of products, and before long still others should be added to the growing list of drugs to control this still unsolved disease.

Colgate Cosmetics

Colgate-Palmolive Company domestic sales for 1955 of $285,577,000, were $23,729,000 higher than domestic sales for 1954. This increase, says the company report, "was contributed primarily by our two largest selling products, Fab and Colgate Dental Cream, and a new product AD. . . . Colgate Dental Cream also recorded a new high in sales and continues to be the largest selling brand in this market. . . . Colgate Dental Cream with Gardol led the Toilet Article Department to a record year. . . . Brisk, a new fluoride tooth paste, has been extensively tested and is now being introduced nationally. Halo and Lustre-Creme continue to lead the liquid and cream shampoo markets. . . . Personal deodorants are now available in many forms and we plan to add an aerosol and stick type to our Veto line."

Chloromycetin Up to $35 Million

Close to $10 million in sales were added to the volume for Chloromycetin in 1955 by Parke, Davis & Company. A jump of 36.5 per cent in sales of this drug brought 1955 sales to $35,180,562 for 1955, compared with $25,774,484 for 1954. Says P.D. president Harry J. Loynd to stockholders concerning this development: ". . . let me emphasize that this increasing use of Chloromycetin by physicians is of far greater significance to our company than the sales volume it represents. This appraisal and recognition of Chloromycetin's true value, and this confirmation of our confidence in it, are daily enhancing the company's reputation and prestige."

A. Ph. A. Plans Expansion

In the midst of its campaign to raise funds for the housing of expanded services to its members, the American Pharmaceutical Association has taken steps to provide personnel to carry on these expanded services.

Dr. H. A. B. Dunning, past president of the Association, who was instrumental in obtaining the site and funds for the present building, is heading a determined effort to raise approximately $300,000 to meet the need for additional office space and other facilities. Dr. Hugo Schaefer, treasurer of the Association, is chairman of a committee to solicit contributions to the A.Ph.A. Building Fund from the membership at large, while Dr. Dunning is personally conducting the drive for funds from the drug industry.

To provide for continued expansion of the Associa-

tion's services in the field of drug standardization, as represented in the publication of The National Formulary, and for the compilation and publication of information and results of researches, on the many scientific and professional problems of American pharmacy, the editorial, library, and laboratory facilities of the Association are being reviewed and will be augmented as funds become available for specific projects.

Dr. Robert P. Fischelis, A.Ph.A. secretary and general manager, has announced a number of staff changes and additions. Chief among these is the appointment of Dr. Eric W. Martin as head of the editorial staff of the Practical Pharmacy Edition of the Journal of the A.Ph.A.

Dr. Justin L. Powers, chairman of the Committee on National Formulary, and editor of the Scientific Edition of the Journal of the A.Ph.A., has also been given the title of Director of Revision of The National Formulary.

Dr. Samuel W. Goldstein, director of the A.Ph.A. Laboratory, is also secretary of the Committee on National Formulary and assistant editor of the Scientific Edition of the Journal of the A.Ph.A., and will continue as one of the associate editors of the Practical Pharmacy Edition of the Journal.

Dr. Robert I. Bischoff, who has been combining responsibility for the production of the Practical Pharmacy Edition with advertising management of both issues of the Journal, will continue as one of the associate editors of the Practical Pharmacy Edition and will give greater attention to the advertising promotion of both publications.

R. E. Dier, a trained librarian, will be given added responsibility for the expansion of the Association's library facilities. George Griffenhagen, acting curator of the Division of Medicine and Public Health of the Smithsonian Institution, who has been for some time the consulting curator of the A.Ph.A. museum, is also engaged in the classification of the Association's valuable historical records and serves in the capacity of convention staff associate.

Paul Parker, incoming president of the American Society of Hospital Pharmacists, will join the Association staff about May 1 as full-time director of the Division of Hospital Pharmacy, which Division is the operating unit for hospital pharmacy affairs and is conducted jointly by the A.Ph.A. and the American Society of Hospital Pharmacists.

Abbott Doings

Abbott Laboratories, in its financial report, states that "anti-infectives, nutritionals, anesthetics and hypnotics, and parenteral solutions constitutes our largest product groups. No one group produces more than 26 per cent of our total sales." The report also says that the sales of the Chemical Sales Division for 1955 were greater than the total consolidated sales of the company in 1933. Also "more than 50 per cent of our current income is derived from products introduced during the past eight years. Products which came out of research in 1955 are contributing well to this year's sales."

Pfizer Settles Fermentation Suit

Chas. Pfizer & Co., in its annual report, tells of the settlement of the suit brought against Pfizer by Ferment-Acid Corporation:

"The action brought against the Company in the amount of $5 million was terminated in February, 1956 by consent of the parties, without liability on the part of either party to the other. The complaint was dismissed on the merits. (Since the Company plans to begin some operations involving processes of the type covered by certain patents owned by Ferment-Acid Corporation, the Company has negotiated a license for the remaining life of such patents, which involves payment by the Company of an aggregate of $220,000 over a period of years)."

This action which was brought in 1954 charged Pfizer with wrongfully using a deep fermentation process originally developed by Dr. Joseph Szucs. Ferment-Acid also charged that Pfizer had improperly used confidential data disclosed by Dr. Szucs during a time when Pfizer investigated the Szucs process under a "look-see" contract. The patent involved in the settlement is U. S. Patent No. 2,353,771, issued in July 1944, and expiring in July 1961.

Ferment-Acid also has pending a similar deep fermentation patent suit against Miles Laboratories, which action charges that Miles wrongfully uses the process in the manufacture of citric acid. This action, also filed in 1954, is for $1 million.

SKF Buying A. J. White, Ltd.

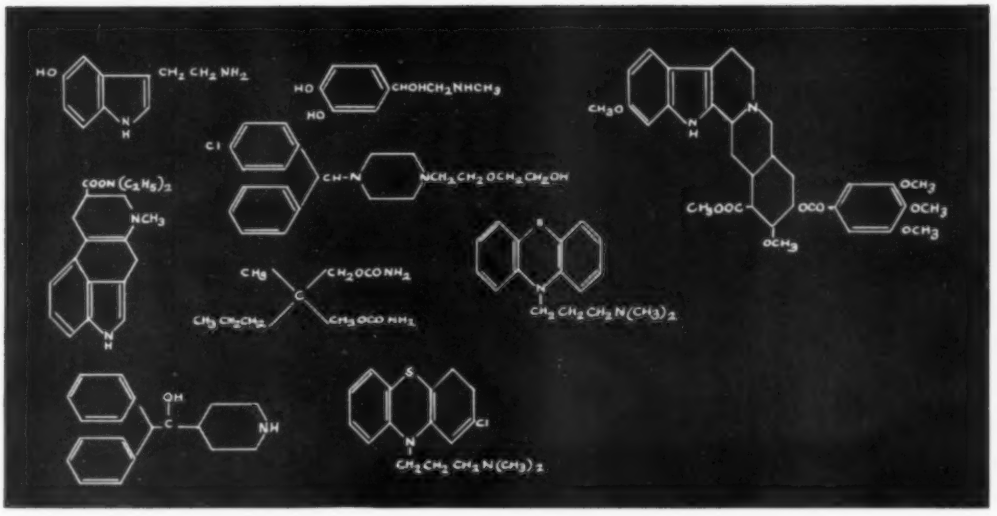
Smith, Kline & French Laboratories announce that their offer to buy all of the outstanding stock of A. J. White, Ltd., London, has been accepted by substantially all stockholders of the British company. The sale price involving nearly 800,000 shares of White stock has been set somewhere in the neighborhood of $2,800,000.

Several subsidiary companies of A. J. White, Ltd., including Menley and James Ltd., London, formerly served as exclusive distributors and manufacturing agents for SKF in various parts of the British Commonwealth. With the conclusion of this transaction, the A. J. White firm becomes a subsidiary of Smith, Kline & French.

Penick Obtains Reserpine Licenses

S. B. Penick & Company have been licensed under the patents of Ciba, Limited, Switzerland, covering reserpine, in all countries where such patents have been issued and where Ciba patent applications are pending. In all countries in which Ciba applications on reserpine are pending, licenses to Penick will automatically become effective as the patents may be issued. Reciprocal license arrangements under patents issued as the result of Penick applications will be considered.

This means that reserpine supplied by Penick to countries in which Ciba patents have been issued may be sold and used in such countries without any conflict with the Ciba patents.



The Race for Mental Health Drugs

All that the pharmaceutical manufacturers of this country need is an indication or a clue that a new and valuable therapeutic agent might be discovered by following a certain line of research, and the chase is on. One has only to recall the time in the mid-thirties, prior to the enactment of the Food, Drug, and Cosmetic Act, when President Franklin D. Roosevelt's son was successfully cured of a serious infection in Boston through the use of Winthrop's Prontasil or Prontylin or both. These were the original sulfa drugs which Winthrop had brought to this country from Germany almost two years before. Up to that time the medical profession had paid very little attention to these drugs. But following the recovery of Roosevelt's son, which news hit the front pages of daily newspapers throughout the country, their use spread like wildfire. And right then and there started the terrific expansion of the pharmaceutical industry which is still continuing some twenty years later.

It will be recalled that immediately following this event, French pharmacologists found out that Prontylin was a chemical called sulfanilamide, a product long known and therefore not patentable. Manufacture of this chemical in this country started on a large scale, and many brands of sulfanilamide became available. However, the shortcomings of this drug, particularly as to side-effects, became known and the search for new and better drugs of this same type started. It is said that more than 5,000 other sulfa drugs were made. Relatively few of these became commercially successful, but products superior to sulfanilamide were the result.

The discovery of the great value of penicillin during the war years, together with the development of mass production methods for this type of drug, together with the development of methods of screening soil samples for possible new antibiotics, set off research activity in this industry to such an extent that it is estimated that over 4,000 antibiotics were isolated in this country, of which only 17 have been placed on the market.

Almost immediately following the development and marketing of the first antihistamine, the industry had available more different products of this type than anyone knew what to do with.

Research touched off by the discovery of cortisone produced similar feverish activity among pharmaceutical researchers, although the number of products thus far made available is not so staggering as it is in the other types of products.

The latest development in this industry, and the one in which every pharmaceutical manufacturer worth his salt is trying to get a foothold, is the tranquilizing drugs. This development at the outset was part of the search for drugs to control hypertension, a search which is also continuing at a high rate of activity. It will be recalled that Rauwolfia serpentina from India was the basis of this entire development. There had been isolated from rauwolfia an amorphous fraction from which Ciba in Switzerland isolated reserpine. This chemical was primarily intended to be used for the control of hypertension, although it was thought by some that it also had a sedative effect. At the time this product was first marketed, other pharmaceutical manufacturers put up products containing the whole ground root of rauwolfia, also to be used for control of blood pressure. However, as reserpine came into use, the tranquilizing effect and its potential use in the control of mental disease became apparent. This use was more or less predicted by the fact that rauwolfia serpentina had been used for centuries in India for mental disease.

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Suntan Preparations

by Harry Hilfer

Suntan preparations, though seasonable products, have been one of the steadiest of the cosmetic items since their introduction. Their development began with the use of mechanical barriers which prevented sunburn by preventing the sun's rays from actually reaching the skin. The mechanical barriers however were not popular since they were difficult to apply and more difficult to remove. The introduction of preparations having incorporated in them compounds capable of permitting certain of the sun's light to come through, and either reflecting or absorbing the light in that portion of the spectrum which caused the principal burning, created a renewed interest in these preparations and caused their sales to rise spectacularly.

These more modern products include substances which are capable of keeping ultraviolet light in the range 2950-3150 Angstrom Units, substantially removed from the skin. This range in the ultraviolet has been demonstrated as being the greatest erythemal effect, since the ultraviolet light of lower wavelengths has been substantially removed by the atmosphere. The light of higher wavelength can produce some erythema, the effects of which are small by comparison. In addition, it has been further demonstrated that the wavelength from 2300 to 3650 produces tanning with a minimum of erythema, so the ideal suntan preparation would contain a screen eliminating light from 2950-3150 Angstrom Units and permitting complete passage of light from the range 3300 to 3650 Angstrom Units. The ability of the effective agent to come as close as possible to this ideal, with the film capable of retaining this property as long as possible, is essentially the method by which any given sunscreen may be evaluated.

It should also be borne in mind that the vehicle in which it is incorporated may sometimes have an additional effect since cosmetic materials, such as mineral oil, have some ultraviolet screening properties and for this reason the sunscreen should be evaluated in relationship to the vehicle into which it is to be incorporated. The screens themselves also vary in cost, but may be evaluated on the basis of use concentration against result. Actually, on this basis the cost of the different agents are surprisingly close to each other. The agencies themselves cover a wide multitude of compounds but practically all of them fall into a class of esters of substituted aromatic acids. These agencies usually have substituents in the ortho position to the carboxy group but not necessarily so, and include esters of salicylic acid, anthranilic acid as well as gallic and digallic acids. Most of these compounds have been adequately tested by their manufacturers to determine optimum concentration and spectral absorptive ranges. There is also an extensive literature available on their irritational characteristics in which a large number are completely safe for use.

The choice of a sunscreen would therefore be highly

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dependent on the type of vehicle into which it is to be incorporated. Of these, alcoholic solutions and cream lotions seem to be the most popular. There are still, however, some preparations whose sole vehicle is a fixed oil such as sesame oil or mineral oil. Though the popularity of these latter vehicles is decreasing, their virtue lies in providing a protective film for the sunscreen against removal by water and at the same time providing a vehicle in which most of these effective agencies may be easily dissolved. An alcoholic solution of the sunscreen is another method of incorporating the sunscreen with the added advantage of providing a non-greasy film. I feel, however, that contrast of the sunscreen without any other barrier to water, as would be the case at the beach, would cause it to be removed much more readily and therefore necessitate more frequent application. Since there are objections to an oily preparation on the beach because of sand sticking to the skin, a happy medium may possibly be reached by using either a low viscosity oil so that the film thickness may be reduced, or by using an alcohol-soluble oil in conjunction with alcohol as the vehicle. Preparations such as the isopropyl esters of fatty acids lend themselves ideally to such a function.

The usual type of emulsion has the advantage of enabling a larger number of substances to be incorporated in it. For example, the choice of an oil need not be governed by viscosity or solubility characteristics, and other substances may be incorporated which would be desirable. Under any other circumstances, this would probably be the ideal vehicle for a sunscreen, but it has the disadvantage at the beach of being more easily washed off by water since the presence of the emulsification agent would cause the emulsion to regenerate if it were allowed to come in contact with water. Fortunately, there are some methods by which the film life of such a system can be extended. One method which could be tried with advantage is by including silicones in the preparation. The silicones are extremely water repellent and many of them, even if incorporated into an emulsion, are not compatible with the rest of the dispersed phase. If a silicone is chosen from this group, it could actually separate itself from the dehydrated film and act as a barrier against waters coming in contact with the emulsifier, preventing the ultimate regeneration of the emulsion and subsequent removal of the film.

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Entire root system of Rauwolfia vomitoria, Belgian Congo.

RAUWOLFIA and its Alkaloids

by E. F. Woodward CHIEF PHARMACOGNOCIST, S. B. PENICK AND COMPANY, NEW YORK, N. Y.

Since early 1946, the pharmaceutical industry has been concerned with the Rauwolfias, most of the activity having taken place since 1951.
The history of Rauwolfia has been well covered in numerous publications. However, the requirements of the medical profession for preparations based on Rauwolfia serpentina and on reserpine have been stabilized to the point where it is possible and desirable to review some of the more commercial aspects and to place them in some perspective.

I. Rauwolfia Serpentina

Status of Supplies of R. serpentina

The principal source of *Rauwolfia serpentina* has been, and still is, the sub-continent of India. It also occurs in India, Ceylon, Burma, Siam, Java, Sumatra, on the Adaman Islands and to some extent in Pakistan, but in practice, commercial quantities would be available only from India, Ceylon, Burma and Siam.

Rauwolfia serpentina obtained from these last four named countries varies from country to country in the relative content of individual and total alkaloids, and this variability has some effect on the biological activity. It is perhaps for this reason that India is far and away the principal source of supply now, although material from the other three countries definitely is usable provided it is properly identified.

In India, *Rauwolfia serpentina* occurs along the foothills of the Himalaya mountains which extend across the northern border of India. The second area

Rauwolfia vomitoria roots being dried, Belgian Congo.

Rauwolfia vomitoria in fruit, Belgian Congo.

in India is along the range of mountains known as the Western Ghats which extend down the west coast almost to the southern tip of India. This is a vast area, and it enables us to say, on the basis of past experience, that India should be able to continue to furnish the world requirement for *Rauwolfia serpentina* for many years to come. Because of the nature of the plant and the manner of harvesting, it is most improbable that the plant would ever become extinct due to extensive collection. However, if there should be any periods of temporary, or even permanent shortage, sufficient root of acceptable quality could be derived from the alternative sources named.

The Embargo

It was in April of 1954 that the now famous embargo was placed on *Rauwolfia serpentina* by the Indian government. Since that time there has been a gradual relaxation to the point where there is no major concern regarding export restriction, and there is practically no control over the export of other species of Indian *Rauwolfia* including *Rauwol.a canescens* and *micrantha*. Although complacency is certainly not suggested, it is now evident that those troubled days are behind us.

Quality

For hundreds of years *Rauwolfia serpentina* has been gathered in India for sale in the local markets in very small quantities, say five or ten pounds at a time. Most of the natives who use the root as a home remedy collect it for themselves in their own environs. So it was entirely natural that there were some difficulties in extending the production into tonnage quantities. Because of the general lack of scientific knowledge of the plant, when it first came to be of interest, there were frequent questions as to identity. Some of these questions can be traced back to the varying usage of common names.

After an extensive effort to educate the collectors there is now practically no question as to what is meant whenever the words "*Rauwolfia serpentina*" are used. To illustrate this point we could mention that collectors in India now use the proper botanical name for the plant and almost never refer to it by the common names which had been in use.

If there is any problem, it is the problem of contamination. As with any material collected from wild growing plants there is always a certain amount of foreign organic matter, the amount being regulated by official or generally accepted standards. For example, as with such drugs as Belladonna root or Aconite root, there will always be a small amount of stem present.

Cultivation

From time to time some thought has been given to the cultivating of *Rauwolfia serpentina* and possibly some of the other species. *R. serpentina* is a small

Rauwolfia serpentina, whole plant with roots.

Rauwolfia vomitoria in the Belgian Congo.

The flowering plant of Rauwolfia serpentina from India.

The fruiting plant of Rauwolfia canescens from India.

perennial shrub; it is a pity that it doesn't enjoy the sort of climate we have here in the United States because it would make a very fine ornamental shrub, something like an Azalea. If cultivation were to be undertaken, the reasons for such cultivation would be 1) to assure continued supply from this hemisphere, 2) to control the quality, 3) for reasons of possible economy and 4) to be prepared if the wild plant should become extinct.

Present informed opinion is that there is little danger of extinction. Secondly, there is almost no suitable climate within the borders of the United States. As for economic reasons, it is most unlikely that *Rauwolfia* could be cultivated as cheaply as it can be gathered in the wilds. Land and labor costs are too high, and the plant is of relatively slow growth.

Nevertheless some attempts have been made at experimental cultivation in India, in the East Indies, in Central America and in the Caribbean areas. At least, if the need should ever develop, there will be the nucleus of experience and propagating materials from which to work.

Prices

R. serpentina as collected by the herbal doctors of India, say ten years ago, used to cost about three or four annas a pound—just a few pennies by our standards. With the advent of tonnage requirements the price rose and assumed a reasonable level, sufficient to encourage production and to provide fair profits all around. Then came the embargo and the price almost tripled.

Within a few months other countries came to be suppliers—at more reasonable levels. Then the embargo was lifted in India, and now the price is back to pre-embargo levels.

There is no foreseeable condition which would greatly affect the price of *R. serpentina* for many months to come.

A Little Chemistry

The chemistry of *Rauwolfia serpentina* and other *Rauwolfias* has interested a considerable number of research workers. At the present time some thirty alkaloids have been isolated from *Rauwolfia serpentina*, and there are probably several more which have not yet been extracted and identified. From a medical point of view, perhaps the most important alkaloid is reserpine, but the action of whole *Rauwolfia serpentina* as opposed to reserpine is claimed to be different and can be attributed to a number of groups of other alkaloids including the ajmaline and serpentinine groups present in the whole root. A number of workers have placed some stress on the presence of the yohimbine-like group also.

It is probable that the relative percentages of these alkaloids varies to some extent throughout the season. It is definitely known that root collected in one geographic location may vary to a greater or lesser extent from roots collected in another location, and it has been shown that the particulars of the handling of the root has considerably to do with the relative percentages of alkaloids appearing in the finished product.

Certain of the alkaloids are of delicate composition and are subject to hydrolysis. It is for this reason that proper precautions should be taken when storing either the crude root or the powdered material or the finished tablet.

At first there were said to be three alkaloids in *R. serpentina*—then 17 or so, now there are over 30 reported. With attention only to those more commonly referred to now, here is an abbreviated classification:

1. Tertiary indoline alkaloids:
   - ajmaline
   - isoajmaline
   - neoajmaline
   - ajmalinine
   - rauwolfinine
2. Quaternary anhydronium bases:
   - serpentine
   - serpentinine
3. Tertiary indole bases of the yohimbine type:
   - reserpine
   - methyl reserpate
   - rescinnamine (reserpinine)
   - deserpidine (raunormine, canescine)
   - yohimbine
   - isoyohimbine
   - serpine
   - sarpagine (raupine)
   - rauhimbine
4. Tertiary indole bases of the tetrahydroalstonine type:
   - ajmalicine
   - reserpinine
   - reserpiline
5. Alkaloids of unknown ring structure:
   - ajmalinine
   - serpenine
   - chandrine

Of these alkaloids, four are available in commercial quantities:—reserpine, raunormine, rescinnamine, and Yohimbine. But of the four, only reserpine is in extensive use beyond the research clinic.

II. The Botanist Vs. the Chemist

Before going further it would be well to clear up one question regarding certain "so-called" species of *Rauwolfia*. At this point we get into the question of taxonomy—the science of naming plants according to the binomial system devised by Linnaeus. In order for a plant to be a valid species it should have certain distinct characteristics, particularly in the flowers, characteristics which differentiate it from all other species of plants. Many of these differences might be considered to be matters of degree rather than of true

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The European FREEZE and Perfume Oils

Mimosa blossoms

The terrifically cold Winter experienced in Europe this year caused havoc with the supplies of essential oils from the major part of that continent. Described as the coldest Winter to which Europe has been subjected during the present century, it has destroyed trees and plants from which fine essential oils are extracted throughout the land. The extent of the damage cannot be completely estimated until the warmer weather sets in.

Perhaps the most serious damage is that brought to the bitter orange trees. From this tree comes Oil of Neroli Bigarde, Orange Flower Absolute, Orange Flower Water and Absolute, Oil of Pettigrain Bigarde (Bitter Orange Leaf Oil), and Pettigrain Water and Absolute.

While the neroli oil, or orange blossom oil, comes from the flowers of the bitter orange tree, the pettigrain oil comes from the leaves and stems. In fact, it is said that even the fruit and twigs of the tree are utilized in oil production. These oils from France and other European regions are of the finest quality and are used for fine perfumes. As an example, pettigrain oil from Paraguay, which country is by far the largest producer in the world, cannot properly be termed a bigarde oil because the leaf material distilled in that country originates from the bitter-sweet variety of orange tree which developed as a hybrid after the

Jasmin blossoms

trees of the two types had escaped cultivation and started to grow wild and semiwild in the interior of South America and Central America countries and in some parts of the West Indies. Likewise the pettigrain oil from Haiti is also a bitter-sweet oil for the same reason. In quality the French oil surpasses all other pettigrain oils, because the producers in Southern France use only the leaves and petioles, eliminating any wooden branches or small fruit. The Paraguay oil and oils of this type, possess a harsher odor than the French oil. For this reason use of these oils is limited to soaps and cosmetics rather than to delicate perfumes.

Harvesting bitter orange (neroli) blossoms

The extent of the damage to the French and other European bitter orange trees can be appreciated when it is realized that the sap goes up through the bark of the tree, and if frost strikes, the bark explodes killing the tree. Furthermore, it is estimated that close to fifty per cent of all the trees may have to be replaced.

After the young bitter orange trees are planted, following development from seeds over a period of two to three years in commercial nurseries, they do not begin to produce until three or four years after planting. For the next ten years the trees produce a normal harvest, the highest yield being obtained dur-

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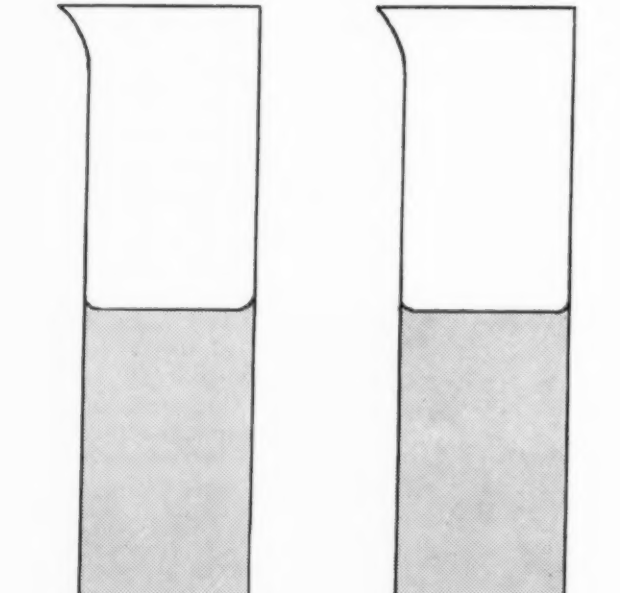
SUSPENSIONS

by Joseph Kalish, Ph.D.



As any experienced formulator knows, whether he is working in pharmaceuticals, cosmetics or specialties, there is more to making a marketable suspension than mixing an insoluble powder with water. Problems usually start with first attempts to wet the powder and suspend it uniformly, continue with efforts to develop desirable properties and then involve maintenance of these properties throughout adequate shelf-life.

A suspension consists of solid particles mixed with, but undissolved in a liquid. When shaken, the suspension must give an appearance of homogeneity; the suspension should then have enough stability so that it will not quickly separate before it is used; as a rule, suspensions will tend more or less to separate on standing but this separation should preferably be kept to a minimum; when the suspension has been allowed to stand for a very long time, without disturbance, as on a store shelf, re-suspension should be possible without major effort.

Fundamental to all theoretical and many practical aspects of suspensions is Stokes's Law, which relates the rate of settling of the particles in a suspension to the radius of the particles, their specific gravity related to that of the suspending liquid and to the viscosity of the liquid. Coarse sand suspended in water settles so quickly that it is quite difficult to make a uniform suspension. As the sand is ground more finely, however, a more uniform and more stable suspension results. It may be possible, although this is quite difficult by mechanical means, to produce such fine particles that the suspension will be stable indefinitely. This is the case when particles are so small that they cannot obey Stokes's law because of Brownian motion. This motion is exhibited when the particles are so small that they show the effect of being hit by individual molecules of the liquid and vibrate or dart about without regard to gravity. In this small size range, colloidal phenomena are predominant and the mixture may take on a new set of properties.

The difference between the specific gravity of the solid and the suspending liquid also determines the rate at which the solid settles (or floats to the surface). If the liquid has substantial viscosity, this, too, will tend to retard the rate of separation.

In making a suspension, the first problem often encountered is wetting the solid. Even when the solid is not intrinsically water-repellent, the process of grinding will often encourage the adsorption of air on

a freshly formed surface and this air layer may retard wetting. As would be expected, wetting agents work perfectly in this situation, reduction of the surface tension of the liquid permitting quick wetting of the solid. For water-repellent substances, more of the wetting agent or a more effective one may be required. Specific dispersing agents, rather than wetting agents alone, will sometimes offer advantages. For the most part, the wetting or dispersing agent used should have low foaming powers. It is sometimes advantageous to pre-mix the solid, the wetting agent and a small part of the liquid vehicle and then dilute with the rest of the vehicle to obtain more effective wetting action. The selection of surfactant, whether nonionic, anionic or cationic and its toxicity will be determined by the properties of the final suspension and its intended use.

The nature of the solid to be suspended is important in determining the nature of the final suspension; the particle size, however, is vital. As the average particle size decreases, particles will settle less rapidly and the suspension will be thicker. To indulge in a bit of mathematics, the distribution of particle sizes making up a given average size will have substantial effect upon the nature of the suspension; if the particles are all of one size the results will be different from those obtained where dispersion of size is great, the average consisting of combinations of small and large particles. The effect of particle size upon viscosity is more notable as the concentration of the suspension becomes greater and concentrated suspensions containing the same weight of solid may be flowing liquids if particles are relatively large in size or thick pastes if particles are small; viscosity will be intermediate if the range of particle sizes making up a given average size is great enough to include a proportion of large as well as small size particles. In concentrated suspensions, particle shapes will be important. Again for a given concentration by weight, particles that approximate small spheres will produce different properties than are obtained when individual crystals are needle shaped, with substantial differences between length and thickness. Finally, as the suspensions become quite concentrated and depart in properties from simple solutions, new factors of thixotropy and dilatancy enter. When a suspension is thixotropic, it is thicker when at rest than after stirring; a dilatant suspension will be more fluid at rest and become thicker when stirred. Dilatancy can be most disconcerting when uncovered accidentally; I recall with no pleasure the long investigation to make a highly concentrated suspension for injection that resulted finally in a surprisingly fluid mixture. This could be pulled up into the hypodermic syringe through a moderately small-bore needle and could then be ejected dropwise. Any attempt to increase the rate of ejection by pressing the plunger more rapidly resulted in jamming and in some instances the syringe was shattered. A dilatant suspension may appear moist and semi-fluid in a beaker but when rapidly stirred with a stirring rod will "grab" the rod and become dry and solid.

The nature of the suspended solid can greatly influence the properties of the suspension. In general, a lyophobic compound, which does not attract or form agglomerates with the suspending liquid, will give suspensions of lower viscosity than substances that do tend to absorb the liquid as a more or less strong physical combination. Thixotropic phenomena are often, but not necessarily associated with physical combinations of solid and liquid. In thixotropy, the individual particles may be assumed to form agglomerates or clusters of particles which extend throughout the mixture (and this is helped by hydration of the particles) and thus substantially increase viscosity. When the liquid is stirred or subjected to some other shearing force, the agglomerates are broken up and viscosity decreases. In dilatancy, on the other hand, the particles at rest in a concentrated suspension are kept apart by like electrical charges on the particles; when stress is applied, however, the particles are too close together to flow around each other easily, pile up into clusters, and higher viscosities result.

Just as the properties of the suspension can be profoundly modified by changes in the physical properties of the suspended solid, so can they also be altered by changes in the suspending liquid. The interaction between the liquid and solid phases will be very different depending upon whether the liquid is aqueous or non-aqueous, polar or non-polar. Since the nature of the liquid, as of the solid, is usually largely determined by the end use of the suspension, room for modification is limited.

Increased viscosity of the liquid will reduce the rate of settling of the suspension; if this cannot be accomplished by the use of a more viscous liquid, then addition of sugar or polyhydric alcohols, where possible, will accomplish the same end.

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Modern Clinical Research

by Irwin C. Winter, M.D.
DIRECTOR OF CLINICAL RESEARCH, G. D. SEARLE & CO.

Not too many years ago the only clinical evaluation of drugs was the total experience of the profession —and of others not of the profession—in the use of that agent in their practice. This procedure, while slow, was successful after a fashion since the materials submitted to such trial and error testing were with few exceptions not only of little therapeutic value but usually quite harmless. This situation does not hold today. Not only are modern drugs potent in the sense of activity but in many instances because of that fact, not at all harmless. Elaborate precautions to avoid the very real possibility of harm to the patient must be established and strictly adhered to in clinical trials of new drugs and of course in their general use. It is not my purpose to describe the type of animal toxicity studies which should be available before a potent new drug is first tried in a human being, but I will emphasize that they must cover the possible hazard to the patient which a new drug by its activity may hold.

Further, a basic rule of clinical research to which we subscribe is that no new drug be given to a patient "just to see what will happen." Administration of an experimental drug to a human subject should be with his knowledge and consent and should have an expectancy of assisting in his welfare. This implies a considerable knowledge of the pharmacologic characteristics of the drug from animal experimentation before it is ever given to a human. Yet animal data, no matter how complete, is of course totally inadequate for routine clinical use. Our problem is to translate this laboratory experience to clinical practice.

On the face of it the most realistic approach to the transfer of animal data to use in human disease is to simply give the new drug to patients suffering from that disease, sit back and watch the results. This is achieved by the time honored "trial and error" method mentioned earlier and there is no question but that properly followed this method will lead to a true conclusion. However, this method is slow, time consuming, and the publishing habits of our fraternity being what they are today, too often leads to the situation where a wave of enthusiastic reports appears, followed by an equally ample wave of critical reports, after which, and several years later, the true place of the drug in clinical practice is determined. In this day of intensive search for new therapeutic agents this process may be repeated many times in quick succession, a circumstance which makes calm decision difficult indeed.

Nevertheless, this method of clinical evaluation is certainly a useful one and is still widely used. If the

drug being tried is sufficiently active and the results sufficiently striking, its work may be quickly ascertained. On the other hand, if more than one drug is submitted to testing by this means, eventual decision may be long delayed.

To illustrate these difficulties, I will refer to our experience in the clinical evaluation of diuretic agents. In the early days of that program, we employed this sink or swim method of immediate trial through the cooperation of a number of clinical investigators. Some of these trials did and do (for we still use them) consist merely of administering the new agent to patients with edema as they appeared for treatment. The efficacy of the diuretic in such a test is determined by the success of the control of the patient's condition, in this case congestive failure. Of course, whether or not the patient was successfully treated might have been due to many factors other than the potency of the diuretic being examined. To control these factors, this type of experiment was made more and more complex by such procedures as eliminating all other forms of therapy (including bed rest) and adding these measures back one by one to determine the effect of those additions on a single patient's condition.

In many trials the patients were hospitalized, placed on rigid metabolic balance, subjected to careful standardization of "other" treatments, kept under these conditions for sufficiently long periods of time to establish a stable state (an impossibility), and eventually trying a single new drug in comparison to a standard diuretic, using first one and then the other in the same "stabilized" patient.

In our early trials, it was not difficult to decide which of our new drugs were diuretic and which were not but it was not easy to select by these means the best of several similar agents. Further, these agents, as do most active drugs, did possess untoward effects which occurred with increasing frequency with increasing dosage. It became more and more difficult to decide whether the diuretic effect produced by a tolerated dose of one of these agents indicated a superiority over other very similar materials and whether, if one could be selected as "best," that superiority was sufficient to warrant its submission to the medical profession. Nevertheless, over a period from 1946 to 1954, through the cooperation of between 10 and 20 excellent clinical research teams throughout this and other countries, it was possible to narrow a beginning list of forty-one such agents to four, and eventually to select one of these four as "best". It was possible to determine an "average" therapeutic dose, to predict the percentage of an "average" population of patients with congestive failure who would respond with diuresis to the drug, and to predict that a certain percentage of these "average" patients would show some degree of "side effects".

As a result of this and similar experiences, it now seems to us much more logical to attempt the evaluation of a new therapeutic agent in graded steps rather than to begin immediately on a full scale determination of the effect of that agent in the treatment of a disease. We believe such a change in method is indicated because drugs today are ordinarily clinically evaluated only if they possess one or more specific pharmacologic activities. The fact that the new agent possesses those activities is determined in the laboratory on animals using well established principles of bioassay. Why not, therefore, first determine whether the human species responds in the same way?

This first trial, which I think we can accurately call "human pharmacology," means that one determines in the human whether a specific effect can be produced, the relationship of the size of the dose and route of administration to the production of that effect, and whether or not that effect can be produced by doses which carry no insurmountable hazard to the patient. For such a program one must determine how an alteration in function produced by the specific action of the drug can be measured in the human with accuracy and how to control the variables which will affect the measurement.

In the case of diutreic agents this problem has been attacked with notable success by Greiner, Gold and their co-workers at Cornell University.[3] These workers selected as an endpoint in diuretic efficacy the simple measurement of body weight and weight loss in response to administration of a diuretic to edematous patients. It is obvious that a relatively tremendous pool of patients must be available in order to select a test group which can be used for these trials. It is also readily apparent that in using an assay of this sort one determines only the relative potency of a given diuretic agent in a very select group of individuals. It cannot, therefore, be considered any more than a guide to the general clinical application of a diuretic. It is solely and entirely a human bioassay to determine the comparative potency of agents having the same pharmacologic action (in this case diuresis) and no more.

This test does, however, give more information than simply a measure of comparative potency. It is possible to record the "side effects" complained of by

(Continued on page 568)

the Tranquilizing Drugs*

by Nicholas A. Bercel, M.D.

ASSOCIATE PROFESSOR OF PHYSIOLOGY
SCHOOL OF MEDICINE, UNIVERSITY OF SOUTHERN CALIFORNIA

Mental health is no picayune matter. Seven hundred thousand patients in this country occupy more than *half* of the available hospital beds. Their care plus the pension paid out by the government to the mentally ill veterans—amounts to one billion dollars a year. And money is the least painful aspect of this problem.

Three hundred thousand individuals are admitted yearly in mental hospitals. *Sixty* per cent of these will leave the hospital in the first year—(though some may be back again), *five* per cent is released after two years, but only *one* per cent after that. *After that* means twenty-six years, the average time spent in mental hospitals by those who have to stay for good.

And we did not even include the cases treated in private practice by the eight thousand psychiatrists—out of a total of close to 200,000 physicians in the United States.

What is the answer to this number one public health problem of our time?

More money for more brick and plaster is obviously not. Custodial care only petrifies the mental illness and makes the building of more asylums more and more necessary. There is only one solution that makes sense. How can we discharge more patients, and preferably within the first year of their illness?

One, and the most important answer to this problem is: more psychiatrists. Attendants and nurses are fine for custodial care, but for discharge you need the doctors. We can learn from the experience of a state hospital in Nebraska. With eleven psychiatrists on the staff—eighty-four per cent of a year's admission could leave within a year. When it lost five, with the remaining six doctors the yearly discharge rate dropped to sixty per cent. But this is only part of the story. Whereas before only 124 patients stood a chance to stay for life, with the reduced staff 421 were destined to remain in the hospitals for good. And, to take care of the extra load of chronic cases, seventy-three attendants had to be hired. There was a saving in salary of $150,000.00—but the Nebraska taxpayer has to spend seven million dollars to take care of the extra load who will stay for life. And again in this horrible story, money is the least painful element.

How can we discharge more patients?

Besides more psychiatrists—now a new ray of hope beacons on the horizon—*the advent of the age of chemistry in psychiatric treatment.*

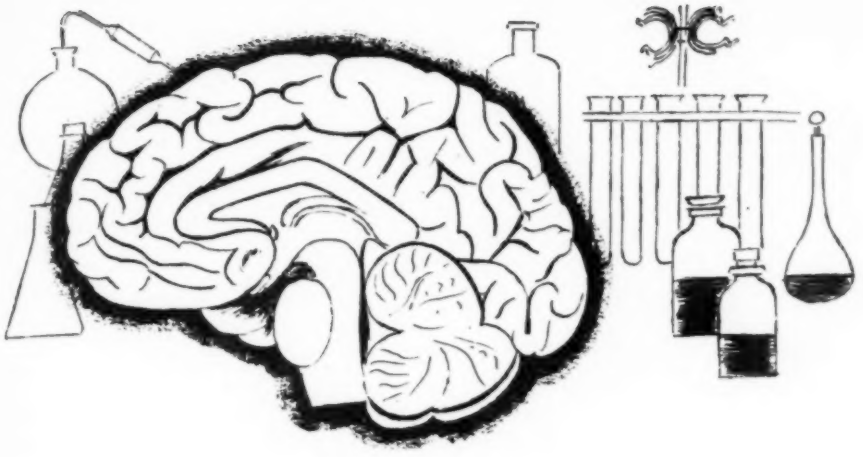
The subject that has been assigned to me at this time has to do with some recent advances in the diagnosis and treatment of mental illness based upon some new acquisitions of a chemical nature which, even though only a few years old, have already produced a minor revolution in this branch of medicine the far reaching consequences of which, at this early time, cannot even be foreseen.

In order to understand the significance of tranquilizing drugs, I suppose it would be best to sketch the background in which they have achieved prominence.

Until relatively recently, the problem of anxiety, agitation and tension, and their consequences, were handled either by drugs that were in many ways inadequate, chiefly because their action was quick without being permanent, or by the slow, laborious and expensive process of psychotherapy which by its very nature was not primarily designed to solve acute problems of anxiety and which often had to compromise with the environmental reality which can rarely be changed radically to satisfaction.

Anxiety can be defined as a physiological state in which the body is geared to cope with an emergency chiefly through the organs which are under autonomous nervous system control. It is supposed to prepare the organism to cope with impending danger either through fight or flight. When the danger is real, known and physical, the sudden upserge of energy mobilized through intricate neuro-endocrine signalization—is used up purposefully and a state of equilibrium calm follows. When the danger is not known, or

*Before Western Section, American Pharmaceutical Manufacturers Association, February 13.



when it is not real, or when it is not physical—it is not possible to use up the energy in either fight or flight. It will consume the individual, hence its unbearable character, its resistance to reason, reassurance; its distorting effect on thinking, on common sense.

Our culture is especially conducive to anxiety. With the acquisitions of technical civilization—physical danger is on the decrease in every day life—while non-physical danger is on the increase. Hence the ever increasing quest for tranquillity, for peace of mind.

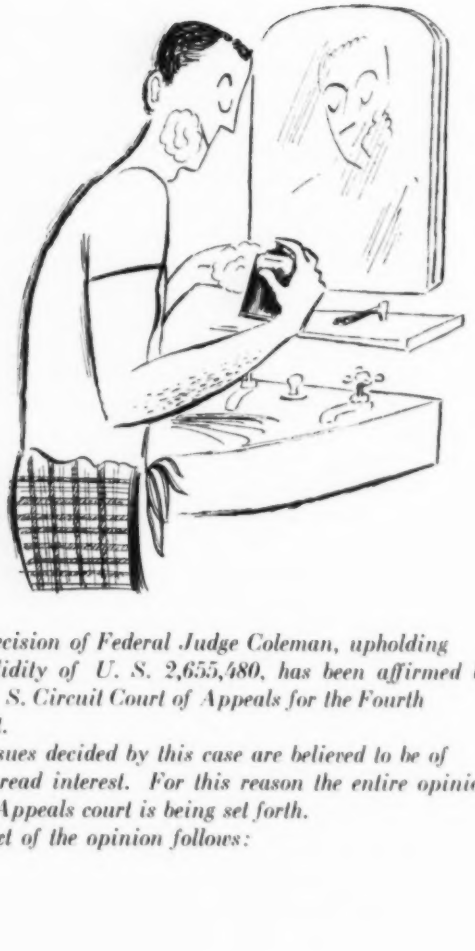
Why were the drugs used in the past inadequate? For the same reason that the housewife has a hard time to remove a spot from the rug, that is, to take out *only* the offending spot, leave no mark and leave the material and its dye intact. Even *effective* tranquilizers *in man* may cause such a disruption in the mental process as to eliminate it due to the *side effects* which were too high a price to pay for the otherwise considerable benefit.

Let us take, for instance, the barbiturates which were widely used prior to the advent of these so-called miracle drugs. If anxiety is due to excitation, it is quite obvious that not all parts of the central nervous system are participating in the physiological process of anxiety. Barbiturates, however, have an overall *generally* sedative quality. Therefore, it was not possible to give it in adequate amounts to decrease or eliminate anxiety without at the same time causing chiefly cortical inhibition which in turn interfered with higher intellectual functions underlying, consciousness, concentration, attention, reactivity to stimuli, abstract thinking, memory processes and such motor functions as underly equilibrium, skilled movements of either the hands, feet and speech. The general impression, therefore, of the anxious individual who was sedated with barbiturates was that he was calm but dull and groggy, he was sleepy, apathetic, and consequently, for the duration of the effect of the drug he was somewhat ineffectual vocationally as well as socially. Let us add to this another liability of the barbiturate, namely, the problem of tolerance and addiction as well as the impermanency of its effects. Barbiturates had, therefore, solved an acute problem on a stop-gap basis, leaving the individual largely an ineffectively functioning man. What applies to barbiturates likewise applied to other sedatives like paraldehyde, chloral hydrate, bromide, and if attempts were made to either eliminate or decrease all the undesirable side effects, this could only be done, generally speaking, at the price of compromising with the anxiety reducing effect of the drug or, to use a housewife's language, if you tried to avoid the circular marks left by your cleaning fluid, if you wanted to save the color, then your spot was not removed completely.

Due to its time consuming and therefore expensive nature, psychotherapy posed a serious limitation on both the number of subjects who could afford to take the treatment and on the number of doctors who were qualified to administer it. Even under ideal conditions, rarely was this treatment capable of solving *acute* problems of anxiety though when, under the best constellation of circumstances, *it was effective in the long run the results had far more permanency than any other treatment known in psychiatry.* But there were other limitations. Anxiety is only a symptom of an underlying psychiatric disturbance the nature of which sometimes makes psychotherapy *impossible to apply to begin with.* Finally, rigid, immovable social, cultural and particularly economic determinants are of such overwhelming importance in some psychoneuroses as to reduce psychotherapy to a device that would help one to *bear* with external realities which cannot be changed. In that sense, therefore, this form of treatment competes with such tranquilizing devices as religion, cults, philosophy, if the individual elected to seek inner peace through belief in the supernatural, or it had to compete with addiction to alcohol and drugs if the subject preferred to *try* to solve his problems by chemical means.

(*Continued on page 564*)

"RISE" Patent



The decision of Federal Judge Coleman, upholding the validity of U. S. 2,655,480, has been affirmed by the U. S. Circuit Court of Appeals for the Fourth Circuit.
The issues decided by this case are believed to be of widespread interest. For this reason the entire opinion of the Appeals court is being set forth.
The text of the opinion follows:

This is an appeal in a case involving patent infringement and appropriation of trade secrets. The patent in suit is United States Patent No. 2,655,480 issued October 13, 1953 to one Spitzer and others relating to a pressurized shaving cream. The plaintiffs in the court below, appellees here, were Spitzer and his partner Small, holders by assignment from the other patentees, and Carter Products Inc., manufacturer of drugs and cosmetics and the holder of an exclusive license under the patent. The defendants below, appellants here, were the Colgate-Palmolive Company, the manufacturer of a pressurized shaving cream alleged to infringe, the Stalfort Pressure-Pak Corporation and John C. Stalfort & Sons, Inc., who packaged pressurized shaving cream alleged to infringe the patent for the Mennen Company, and the Read Drug & Chemical Company, Inc., which sold the pressurized shaving cream for Colgate and Mennen. Plaintiffs claimed infringement of only eight claims of the patent. Defendants admitted infringement if these claims were valid but denied their validity and asked judgment declaring them as well as all other claims of the patent invalid.

The trial court held the patent valid, and enjoined infringement thereof as well as the use of a trade secret held to have been wrongfully appropriated by Colgate. It also ordered Colgate to assign to plaintiffs rights under patent applications found to have been based upon the trade secret. The case was referred to a special master to determine and report as to damages resulting from infringement and also as to damages and profits for which Colgate should be required to account because of misappropriation of trade secrets and to make recommendations as to whether the damages on account of patent infringement should be increased as allowed by statute, reserving, however, for future determination the question as to whether increased damages should be awarded. Judgment was entered that plaintiffs recover their costs and taxable disbursements to date, including against Colgate reasonable attorneys' fees, and the special master was directed to include in his report a recommendation as to the amount of attorneys' fees to be allowed. Three principal questions are presented by the appeal: (1) Is the patent valid? (2) Should the findings of the trial court as to misappropriation of trade secrets be sustained? And (3) Is the decree proper?

upheld on appeal

1. The Validity of the Patent.

Spitzer, one of the patentees, in the year 1948 conceived the idea of developing a shaving lather which, like the lather produced by machines in barber shops, could be used as it came from the container without being worked up on the face. He employed Foster D. Snell, Inc., consulting chemists, to work out his idea for him in terms of a mixture that could be enclosed in a small container and, upon the opening of a valve, would emerge in the form of a durable lather, which, without whipping up or other agitation, could be used for shaving purposes. Snell put to work on the project two chemists. Reich and Fine, who after several months of work and experimentation developed an emulsion consisting of an aqueous soap solution mixed with certain gases liquefied by pressure, which they enclosed in a container. When the valve of the container was opened the pressure of the gases extruded the emulsion and, as it came from the can, the particles of gas expanded into minute bubbles covered with soap which was the shaving lather desired. Patent, applied for November 2, 1949, was issued to Spitzer, Reich and Fine October 13, 1953. In the meantime an exclusive license had been granted to Carter and the product was being marketed under the trade name of "Rise." It achieved at once outstanding commercial success. Sales of "Rise" in 1950 amounted to $400,000, in 1951 to $800,000, in 1952 to $1,800,000 and in 1953 to $2,600,000. The sales of Colgate's infringing product in 1954 amounted to $5,000,000.

There was, of course, nothing novel in the use of soap to make lather, nor in the use of a can as a container, nor in the use of a gas liquified by pressure and mixed with another liquid to spray the mixture from the can. What was novel was to get a mixture of the right gases, with the right soaps in the right proportions, confined in a container under the right pressure, so that a lather satisfactory for shaving purposes would be produced when the mixture was allowed to emerge. In producing such a mixture many problems were encountered and the record shows that their solution took many months. The first experiment consisted in mixing a liquid soap then on the market with nitrous oxide gas, the gas used with pressurized whipped cream. This was a failure because the gas was soluble in the aqueous soap solution and the product extruded from the container was not a lather useful for shaving but a mere soapy liquid. An emulsion consisting of the gas propellant Freon-12 (dichlordifluormethane) and the soap solution used in barber shop machines would not do because the pressure was too high. Reduction of the vapor pressure by mixing Freon-11 (monofluortrichlormethane) with Freon-12 produced a smarting, skin-irritating product not suitable for shaving. Reduction of vapor pressure with mineral oil solved the pressure problem but produced problems in connection with the soaps. Finally, after much experimentation sodium soaps were eliminated and the soap solution adopted was a combination of 80 parts of TEA (triethanolamine) stearate and 20 parts of TEA cocoate, to prevent jelling. The proper propellant was found after much inquiry and experiment by mixing Freon-114 (1, 2 dichlor 1, 1, 2, 2 tetrafluorethane) with Freon-12. The trial judge summarized the matter as follows:

> "Precisely what is this new combination? The individual ingredients of the shaving soap solutions embraced in the Spitzer patent were old in the art. So were the Freons. Also, Freons had previously been used successfully as propellants in aerosols and insectic des. In other words, the *combination* of some Freons with the Spitzer soap solutions was not new in the art But the combination of an aqueous soap solution, emulsified in the liquid base with a Freon which had not only low water solubility but which combined the properties of (1) not smarting or burning the face, and (2) good, stable lather, was unknown. There were a number of Freons used in the propellant art which did not smart or burn the face, but they did not afford a good stable ather. Conversely, there were those Freons that were known to give a satisfactory lather but they were disagreeable on the skin. It is this combination of a relatively small group of Freons, that manifest those desirable properties of low water solubility and the optimum characteristics of non-smarting and of lather quality, with aqueous soap solutions that constitutes the invention of Spitzer and his associates. They discovered that all three of these characteristics were inter-related. They found that Freons having a solubility in water not exceeding about 32 cc. of gas to 100 grams of water to be the type of Freons productive of the optimum of the other two qualities desired in the lather composition. This is what the specifica-

tions of the Spitzer patent teach, and all eight of the claims in suit are responsive to this teaching. Claims 6 and 9 are limited to the use of Freon-114. Claims 8 and 10 are limited to the use of Freon-12. Claims 18 and 20, which are based upon claim 16 as a parent claim, prescribe the use of any one of a group of five Freons, including 12 and 114. Claims 8 (based on claim 2) and 15 embrace the use of a broader group of Freons, but in this group also are *only* Freons that are essentially non-smarting to the face, and stable in lather forming. In fact, the entire 21 claims of the patent are so limited."

The invention is thus described in the specification:

"In general, the above and other objects of the invention are carried out by employing a composition comprising a water solution of a suitable soap or like detergent and a highly volatile organic liquid, hereinafter generally termed a propellant. At least a substantial proportion of the propellant used in the mixture is insoluble in the soap solution and the two primary ingredients are mixed and maintained under sufficient pressure so that the insoluble portion of the propellant is in liquid phase, existing as droplets or in the form of a liquid-liquid emulsion in the soap solution. The mixed primary ingredients are confined at the vapor pressure of the propellant in a pressure-tight container having an opening controlled by a suitable manually operable valve. When the valve is opened, the pressure on the composition is released as it emerges from the container, with the result that a fine textured creamy lather is produced. The action is apparently such that the volatile propellant liquid, entrapped as an emulsion within the liquid soap solution vaporizes upon the release of pressure therefrom, forming fine gas cells throughout the liquid soap solution and thus forming it into a lather."

Of the claims in suit, claims 2, 6, 10, 16 and 20, may be taken as typical. They are as follows:

"2. A package comprising a pressure-tight container having a valve-controlled opening and containing a composition for use in producing a stable lather consisting essentially of a liquid mixture of an aqueous soap solution and a volatile propellant in liquid phase, the composition being confined in the container under the vapor pressure of the propellant, said soap solution comprising a solution which is non-gelling at room temperatures and which contains at least about five per cent and not substantially exceeding about 30 per cent by weight of soap, a substantial proportion of the soap in said soap solution comprising at least one soap selected from the group consisting of the soaps of potassium, sodium and the water soluble aliphatic amines, said propellant being a halogenated alkane having not more than two carbon atoms and containing at least one fluorine atom, the atomic weight of each substituted halogen atom not exceeding 36, the proportion of propellant being from about 0.2 to about 0.0125 mole per 100 grams of the composition, said propellant having a vapor pressure in the range from about five to 300 pounds per square inch gauge at 70 degrees F and having a solubility in water not exceeding about 32 cc. of gas to 100 grams of water at atmospheric pressure and 25 degrees C.

"6. A package according to claim 2, in which a substantial proportion of the soap in the soap solution comprises triethanolamine stearate and the propellant comprises 1, 2 dichlor 1, 1, 2, 2 tetrafluorethane.

"10. A package according to claim 2, in which the soap in the soap solution comprises at least 30 per cent triethanolamine stearate and the propellant comprises dichlordifluormethane.

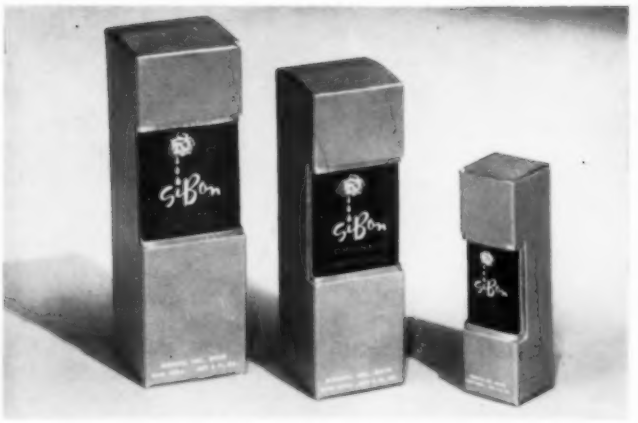
"16. A package comprising a pressure-tight container having a valve-controlled opening and containing a composition for use in producing a stable lather consisting essentially of a liquid mixture of an aqueous soap solution and a volatile propellant in liquid phase, the composition being confined in the container under the vapor pressure of the propellant, said soap solution comprising a solution which is non-gelling at room temperatures and which contains from about five per cent to about 18 per cent by weight of soap, said propellant comprising at least one compound selected from the group consisting of the substantially water-insoluble fluorinated-chlorinated ethanes and methanes in which all of the hydrogen atoms are replaced by chlorine and fluorine and in which the number of fluorine atoms in the molecule at least equals the number of chlorine atoms, the proportion of propellant being from about .07 to about .025 mole per 100 grams of the composition, said propellant having a vapor pressure in the range of from about 15 to about 65 pounds per square inch gauge at 70 degrees F.

"20. A package according to claim 16 in which the propellant consists of a mixture of dichlordifluormethane and 1, 2 dichlor 1, 1, 2, 2 tetrafluorethane and in which the soap in the soap solution comprises a higher saturated fatty acid triethanolamine soap and includes a lesser proportion of sodium soap."

The defendant Colgate-Palmolive became interested in a pressurized shaving cream when "Rise" came on the market; but although it had 200 or more chemists at its service and although it purchased packages of "Rise" and had them analyzed, the record shows that it was unable to develop a satisfactory product until it had employed Fine, who had been working for Snell in the development of "Rise." He gave Colgate the formula which brought success to its efforts and which

(*Continued on page 554*)

CARTON AWARDS 1956



Winner of honorable mention in the cosmetic category: Monico's Si Bon.

Winner of honorable mention in both the cosmetic and display divisions.

Winner of honorable mention in the cosmetic category: Courtley Cosmetics.

America's best cartons received awards at the annual convention of the Folding Paper Box Association held last month. The winning cartons for 1956 were selected from a record breaking total of 7,027 entries from all fields. Winners were selected on a basis of technical quality as well as on such general merits as product protection, display value, merchandising value, practicability, and structural style.

The new packages shown this year clearly indicate the consumer buying shift to self-service and self-selection, said Gustav L. Nordstrom, executive secretary of the Association. Product manufacturers and box makers are gearing packaging to the prediction that by 1960 one out of every three stores will have self-service or self-selection to a major degree. "The trend to multi-color packages is also noticeable," said Mr. Nordstrom. "There has been a definite upgrading of quality and durability in both printing and construction."

Catering to consumers' wishes and even keeping a few steps ahead of them was the business of packaging, said Mr. Nordstrom. It is reflected in the emphasis, by paper box manufacturers, on easy openers, multi-packs, gift boxes, and multi-packs of related items.

The first award in the cosmetic and perfume category was won by John Hudson Moore Company for see-through window single and double-unit gift cartons which take advantage of the quality artwork on Sportsman cologne and after-shave lotion bottles.

LIPSTICK TRACES

THROUGHOUT THE WORLD

LEAVE A BRILLIANT TRAIL

OF BEAUTY FROM

PLUME & ATWOOD

Lipstick Cases

THE PLUME AND ATWOOD MANUFACTURING COMPANY • THOMASTON, CONNECTICUT

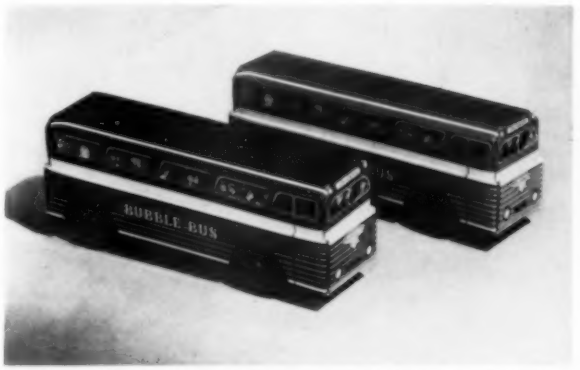
Winner of the first award in the medicinal products division, Delfen Vaginal Cream, center, is surrounded by merit award winners: clockwise, Burn-O-Lin, Kaopectate, Evenflow Family, and Tetrazets.

Glued double hollow side cells cushion the bottles during shipment.

The first award in the medicinal product division was won by Ortho Pharmaceutical Corporation for its carton for Delfen Vaginal Cream.

Other winners in the medicinal products division are Upjohn's Kaopectate which won first in the multicolor letterpress category and honorable mention in the medicinal products and display containers categories, Pyramid Rubber Company's Evenflo Family, George H. Rundle Company's Burn-O-Lin Ointment, and Sharp & Dohme's Tetrazets Direct Mailers, all of which won honorable mention in the medicinal products category. Shoron Optical lenses of Modern Optics, Inc., won honorable mention in the miscellaneous category.

Other winners in the cosmetic and perfume category are: Monico's Si Bon, and Lee Limited's Courtley Cosmetics for Men which won honorable mention in the cosmetic category; Colgate-Palmolive Company's Palmolive for Men which won honorable mention in both the cosmetic and display container divisions; Bubble Bus of Tom Fields, Ltd., which won honorable mention for construction; Avon Family Products which won honorable mention for two-color letterpress; Helena Rubinstein's Jazz and Gillette's Prom Permanent Wave Family which won honorable mention for lithography.



Winner of honorable mention for construction: Bubble Bus, Tom Fields, Ltd.

Winner of honorable mention for lithography: Helena Rubinsteins's Jazz.

Why packaging in polyethylene sells more drugs and cosmetics

Hundreds of containers are improved with new beauty, new convenience, new safety!

In packaging drugs and cosmetics, no trend has been so far-reaching, so spectacular as the trend to polyethylene.

Today this versatile plastic is giving hundreds of drug and cosmetic products a fancy new dress which increases glamor at point of sale and increases utility in the home.

As an important supplier of the resins from which polyethylene packages are made, Monsanto here reports on some of the outstanding developments.

Polyethylene is now packaging powders and liquids, crystals and creams, hard goods and soft goods. Bottles, cans, tubes, vials and transparent packets are being fabricated from polyethylene at low cost. Its coloring characteristics make it ideal for high-fashion containers. Its light weight lowers shipping costs. Its flexibility eliminates breakage.

And user benefits are endless. Powders and lotions can now be neatly applied by "puffing" a polyethylene bottle. Liquids can be squeezed out drop by drop from a polyethylene container that doubles as a dispenser. Precounted capsules and tablets in a polyethylene film bag save the time of druggist or pharmacist in filling prescriptions.

Monsanto will be glad to put you in touch with packaging specialists who will work with you on your requirements. Write Monsanto Chemical Company, Plastics Division, Room 1231, Springfield 2, Mass.

Talk to Monsanto about packaging your products in

Monsanto *Polyethylene*

MONSANTO

Monsanto also supplies styrene and cellulose acetate for profitable packaging.

Silver Award winner: Procter & Gamble's Crest Tooth Paste.

Variety Store Package Awards

Gold Award winner: Jergens' "Tear Drop."

Gold and silver awards symbolic of outstanding achievement went to 21 leading variety store suppliers last month in the annual competition sponsored by Variety Store Merchandiser. The judges selecting the winners were C. R. Trethaway, buyer for Woolworth; H. E. Mertins, divisional merchandise manager for Kresge; L. C. Shockley, vice-president sales promotion for McCrory; N. L. Jones, buyer for Kress; J. H. Frick, merchandise manager for Newberry; and J. Gordon Lippincott, industrial designer.

Of the seven categories of products for which awards were made, the only one of interest to this industry is Cosmetic and Toilet Goods Division. Three awards were made in this category.

The Gold Award went to Andrew Jergens Company for its Jergens Lotion "Tear Drop" package designed by Donald Deskey Associates. The bottle is made by Tygant Valley, and the label by Reynolds Metal Company.

Silver Awards were made to Procter & Gamble for its Crest Tooth Paste package designed by Donald Deskey Associates, in a tube made by Wheeling Stamping Company, and a carton by Richardson Taylor-Globe; and to Hazel Bishop Company for its Hazel Bishop Compact Make-Up package designed by Raymond Spector Company, with card by Lord Baltimore Press.

Silver Award Winner: Hazel Bishop Make-Up.

These flint glass bottles are from our C-39 line . . . one of our most versatile and attractive styles. Available in either clear glass or frosted and can be supplied plain or with your own fired-on ceramic label. Made in 14 sizes from 1/2 dram to 16 ounce capacity.

CARR-LOWREY GLASS CO.

Designers and manufacturers of fine glass containers

Factory and Main Office: BALTIMORE 3, MD. • New York Office: 415 MADISON AVE. • Chicago Office: 1572 MERCHANDISE MART

for repeat sales

COMPLEMENT BOTTLE BEAUTY with this RISDON valve's BEAUTIFUL SPRAY PERFORMANCE

- Wider cone, finer, drier spray cloud and longer lasting contents promote customer satisfaction and brand loyalty.
- Applicable to both 2-phase and 3-phase spray products in either coated or uncoated glass, plastic or metal containers. Special actuator design gives top quality performance on virtually any pressurized product including ultra-low pressure products, water-base products and products not soluble in propellant.
- Permits greater formulation latitude – minimizes propellant – facilitates elimination of dilution effects on fragrance or other qualities of product.
- No metal in contact with contents – No spring – Instant "on-off" action. Vertical or Horizontal spray. Also available with foam actuator.
- Available with custom-designed metal or plastic caps.

contact Risdon for further details and free operating samples . . .

RISDON

THE RISDON MANUFACTURING CO.

H-71

Packaging and Selling

Expert Doesn't Like Perfume Advertising

Among the most controversial advertisements ever run by this industry, "and that's saying something," is the cartoon series now running in "Beauty Fashion" and "The New Yorker" for Angelique perfumes. As a sample of the kind of emotions this advertising is stirring up, we quote from an article in a recent issue of "Advertising Age" written by a current advertising consultant, who, for many years, had been in charge of creative activities for one of the largest advertising agencies.

This expert revolts at Angelique advertising with a display of verbal fireworks which is worth recording for this industry. As a premise for this emotional outburst, this distinguished advertising man lays down the following pronouncement:

"One of the essentially psychological techniques employed to influence the actions of people, according to investigators of the phenomena of human behavior, is the very simple device of linking the product with some symbol or value already known to them and likely to effect favorable emotional reaction." Examples cited are the Rock of Gibraltar as an established symbol of enduring strength and dependability for the Prudential Insurance Co. of America, Rastus for Cream of Wheat, Log Cabin for molasses and syrup, the Old Homestead for ham and bacon and many other symbols.

As further authority and just to make the opinion conclusive for this particular advertising technique, there is reference to that standard authority "Foundation of Psychology" published by John Wiley & Sons. There is one thing that is just not completely conclusive about this analysis, and that is that Angelique is one of the conspicuously and consistently successful companies in the perfume trade in the last ten years. The second is that this behaviour approach of poking fun both at themselves and at the perfume business is not new and is not an untried formula. Some people may remember the article which appeared in "Life" several years ago about the perfume company located on Skunk Alley and some of the illustrations to this article, which showed the versatile and thoroughly unorthodox principals of this company, that is Charles Granville and Lee Swartout, obviously having a good time dressed in big skunk skin caps. While this article in "Life" horrified a large part of the perfume industry and aroused some fear that there would be a deep injury to the entire industry from this article, the facts are that Angelique perfumes took an enormous jump in sales volume and no perceptible harm came to the industry or any other company that was ever individually noted or commented on.

As for this particularly unique advertising series appearing in "Beauty Fashion" and "The New Yorker," there has been a great deal of comment and interest in the trade as well as from the consumer. Far from blasting any precious myth concerning the fragile preciousness of these perfume products, there has been a great deal of specific evidence of both trade and consumer interest together with an increase in business and the opening of new accounts which the company believes could only have resulted from this advertising.

So far as we have been concerned, as a fairly large buyer of life insurance, the Rock of Gibraltar has always left us completely cold, nor did we ever have the slightest fear or suspicion for the integrity or stability of other established insurance companies that happen to attract our attention in some other way. Also, we have an unfortunate yearning for wheat cakes flooded with maple syrup, but we do not ever remember feeling the slightest compulsion to use Log Cabin syrup because of any association with the symbol of a log cabin. However, to get back to our expert, who evidently has very conscientiously read this book on psychology and taken it to heart, we take pleasure in quoting his words as an excellent example of unequivocal disapproval.

"The question I wish to propound is this: If linking a product with *good* symbols creates a favorable emotional reaction, doesn't it follow that linking a product with *bad* symbols is likely to create an unfavorable emotional reaction?

"Specifically, I now call your attention to the Angelique page ad, shown here. Angelique, it seems, is "the scent of the Cognoscenti," and, no doubt, it retails to the said Cognoscenti at something like fifty dollars the ounce.

"Now, I ask you, have you ever, in all your born days, laid your eyes on a more gruesome collection of nauseating symbols—the Skunk Works, the repugnant old witch, the odious brat, the fatuous old man crushing with his nasty feet that evil-looking tubful of piscatorial bad dreams?

"Sure, this frightful page is an extreme example of imbecility. But, aside from the fact that it is exceptionally loathsome, it is representative of the crimes that are today being perpetrated in the name of advertising by a certain limited school of alleged admen."

Still Holds

Here's an observation that still applies with intensive force even in these days of multi-million dollar television advertising commercials.

"I want to emphasize that there is no magic in advertising that will overcome the absence of merchandising at the retail level—none whatever." Ade Schumacher, President, Liggett-Rexall.

Deodorants

More than any other cosmetic product, the deodorant has become a purely functional product. Almost entirely, the advertising copy for deodorants has avoided the strictly feminine, glamorous approach and gotten down to blunt reason why copy. Probably this is logical because the deodorant is frankly purchased to perform a specific function, and if it does not perform that function properly, there is very little else that can be said in its favor.

Deodorant sales have been among the most dynamic in the cosmetic industry over the last 10 years. This dynamic growth is evident in the expanding sales of the leading brands, as shown by the increased promotions, advertising, and package purchases. The growth of this product has also been shown by the continuing entry of new brands, a high percentage of which establish a permanent place for themselves.

The growth however has not been quite as dynamic as the surveys of magazines and newspapers show. Most of these surveys show both men and women using a deodorant with a frequency greater than the use of any other cosmetic (that is of course excepting such toilet preparations as tooth paste and shaving cream) and they also show a minimum of 80 per cent of their readers using the deodorant. As a matter of fact, we just recently saw a magazine survey which claimed that 98 per cent of their readers were using a deodorant.

What this means, of course, is something very elementary in human psychology. There are very few people when asked a blunt question, "do you use a deodorant?" either in a personal interview or a questionnaire, who will fail to say that they do use a deodorant. The alternative, even though true, is a little bit offensive to almost everybody's ego.

In spite of all this trend to functionalism, and the blunt practicality being used by the public in buying a deodorant, there is one cosmetic company, that is Bourjois, who are giving up the blunt appeal and are going into a large list of women's magazines with the traditional cosmetic sales approach. This advertising copy will show a somewhat exotic looking young lady and a somewhat dreamy looking young man with an ad line, "Have a breath of Paris about you—every day."

Maybe this positive approach, that is progressing beyond the mere absence of odor and offering a plus positive odor will make a new appeal. Maybe deodorants can come back to the cosmetic industry, the industry that deals in positive pluses in appearance, glamor or fashion.

Premiums

American business has been constantly giving away more of something else in order to sell what they have themselves.

According to the trade magazine, "Premium Practice," there were 45.7 per cent more contests last year than in 1954 and 32.8 per cent more than in any other year up to the previous high of 1948.

The food field which took the case, so to speak, is reported in this survey to have spent 421 million dollars last year on premiums and prizes.

Pungent Selling

It has long ago been proved in selling that when a visual demonstration accompanies a sales talk that the percentage of sales made and the amount per sale substantially increases. It was undoubtedly with this thought in mind that the Division Managers of the Norwich Pharmacal Company, gathered in meeting to discuss the rapidly mounting sales of NP-27, their new fungicide for athlete's foot, decided to give a realistic atmosphere to their gathering.

We have had no release as to whether these managers expect the salesmen to carry out this kind of a demonstration. If so, it will probably require the invention of zipper shoes. This sort of a sales demonstration should also prove quite an impetus to air conditioning in drug stores.

NP-27 is sold in an attractive green polyethylene squeeze bottle with a white cap.

In this picture of pungent selling, the managers from left to right are J. J. Massenbrock, W. D. Woodburn, E. L. Violon, R. E. Le Blanc, Mr. Zimmermann, Noble Reeves, Donald Mansmith and R. A. Kaiser.

Fragrance Promotion

Houbigant has under way a promotion for Quelques Fleurs fragrance that looks like one of the big promotions of this year. This promotion developed from a happy linking up of the name, which means "Some Flowers," and a news note in a travel magazine which reported that one of the three major interests among tourists in visiting France was to see the formal French gardens which are so famous in Europe.

Houbigant has had designed by a leading American nursery man a model French formal garden. The plans for this formal French garden, with a packet of selected seeds, have been offered to the 12,000 garden clubs in America as a contest. We hear that the responses have been considerably beyond the hopes of the company and that the leading department stores to which this promotion has been offered are showing a keen interest in a tie-in with garden club activities. It is nice to see an old, respected fragrance like Quelques Fleurs promoted with such an interesting, original idea and one which appeals to such a considerable group of American women.

TV Abuses

According to recent comments from Congress, the Better Business Bureau, and particularly, the Federal Trade Commission, television is heading for some pretty blunt and critical investigations.

Lowell B. Mason, senior member of the Federal Trade Commission, is a man who has minced no words on several public occasions. Turning to television he recently said:

"The American home is being deluged from morning to night with spurious TV-radio advertising claims, gimmicks and the clamor of the shills. With the tremendous force exerted by this merchandising evident, we no longer can assume that the abuses are trivial and will be corrected somehow, some way, some time by somebody."

Mr. Mason continued, "Air-borne hucksters have irked not only reputable merchants and indignant citizens in the drive for a 'fast buck' but TV and radio station owners themselves are confronted with corner-cutting competitors and are vehemently demanding protection. The public wants to know if a product is recommended by doctors or by a shill wearing doctor's white coat.

"It wants to determine if 'give-aways' and free offers are either free or given . . . and for how much.

"I'm personally so allergic to TV that I only tune in certain programs where I'm fairly sure I won't be 'put upon.' I imagine millions of viewers feel as I do."

I consider gimmick-selling—a broad term covering bait advertising—today's greatest merchandising evil. A lot of responsibility for gimmick-selling and its abuses rests on the shoulders of big give-aways like the $64,000 question.

Nearsighted Shopper

A few issues ago we cited a statement by a package designer pointing out what must certainly be a primary problem in packaging and yet one that has been almost completely ignored.

This package designer, Frank Gianninoto, stated "A majority of women shoppers leave their glasses home or will not wear any. As a result, a successful package must stand out from the blurred confusion the shopper encounters in any store."

We are interested to note that a meat packer, Stahl-Meyer, is redesigning their packages to lure the nearsighted shopper.

Our Problem

"Our problem is no longer one of production, but of consumption," according to a leading market research expert. "It is not a question of satisfying needs—these are already satisfied," states this expert. "The problem is in satisfying wants and it is not a matter of satisfying only present wants, new ones must be constantly created."

"The economic difficulties of other countries stem from their lack of motivation to better themselves." "They sit in poverty on bags of gold as they have done in China, India and Russia for centuries," this expert concludes. Their resources are fabulous, but little use has been made of them.

Broadening Aerosol

"Inside the Consumer Aerosol Market" is a new, comprehensive market survey by Du Pont which is well worth study by anyone in this trade now using aerosol or planning to use it or even playing with the idea in their mind.

The products of this industry which are now packaged in aerosol and which are included in this survey are: Room Deodorant, Hair Spray or Fixative, Shaving Cream, Hair Conditioner or Dressing, Personal Deodorant, Perfume, Cologne and Toilet Water, Hand Lotion, Sun Tan Lotion, Hair Shampoo, Burn Spray, and Athlete's Foot Remedies.

This substantial product coverage shows this particular industry to be far out in front as the number one user of aerosol packaging. In addition to this, a number of incidental users who do not seem to be included here, particularly from the pharmaceutical field, make it particularly clear that industry will increasingly hold its lead as the industry making the broadest use of aerosol dispensing for its products.

Gold Advertising

John H. Breck Company will be the first advertiser in the "Ladies Home Journal" to utilize the new Curtis metallic inks in introducing its new spray net products.

Ed Breck, in making this announcement, pointed out that the use of metallic gold ink closely approximates the Breck package in its maximum package identification in their advertising.

New Package Combination

Polyethylene and tin are combined to make a new, squeezable container. This package recently introduced by the Bradley Container Corp. uses polyethylene walls with a metal seal at each end. This container is under test, according to reports, by Breck's, a Boston mail order house for a spray dust insecticide and by Colgate for a liquid detergent.

New Cosmetic

A new cosmetic product, especially for the feet, has just been introduced by the Kendall Company, Blue Jay Sales Division. This is Fling, an anti-perspirant powder packaged in a plastic squeeze bottle.

Fling is intended to keep feet dry, deodorized and fresh all day. This is the kind of a product that puts the cosmetic industry in the business of personal care from head to foot.

Things to Come

A professor from the University of Maryland's Physics Department thinks that the new earth satellites, that is the small man-made moons that scientists are developing, should be used for advertising. He stated "it is quite possible to visualize the satellite as a type of advertising medium built and owned by a corporation and leased to various advertisers." "You could have a receiver, a tape recorder and a transmitter." "The message which it transmits could be changed from time to time at the discretion of the man who owns and leases the satellite."

Notes and Comments

A great many people in this industry think that Charles of the Ritz has the most successful policy or formula for selling in the entire part of the cosmetic industry using selected distribution.

A basic part of the Charles of the Ritz formula, and probably the pivotal point on which their whole system of retail franchise has revolved, has been the made-to-order face powder which was first introduced to the retail trade 25 years ago.

Now, for the first time, women can have their made-to-order face powder pressed into cake form before their eyes at the Charles of the Ritz cosmetic bars in any one of the retail stores that they have franchised.

This made-to-order pressed cake form of face powder is made possible by a small chromium, hydraulic power press which can be used right at the retail counter by the Ritz demonstrator. If this little machine does nothing else, it is bound to add interest and fascination to cosmetic customers who stop at a cosmetic department where a demonstration is taking place.

We are under the impression the polyethylene bottle is beginning to make strides among drug and pharmaceutical manufacturers. Just within the last few days we have noted the adoption of the polyethylene bottle by Johnson and Johnson and Norwich Pharmacal. Since this branch of the industry is one of the major users of glass containers, "Poly" has an increasing market potential in this field.

The new package which Ciro is using for their aerosol dispenser cologne series is a wonderfully designed glass container, with really beautiful pastel shades of coating on the container. We understand that this is a Wheaton glass job and we think it is a luscious and magnificent way of decorating a glass container.

We like the article in "Tide" about Roger & Gallet. This is one of the finest and oldest companies in the trade, and it is a pleasure to read an article outlining such aggressive progress as this company made during the last year, and anticipates making this year. A little over a year ago, President Guy Rocherolle took on two new people who have had a great deal to do with this new growth. One of these was Bob Buckalew, who has put a great deal of energy and vision into sales management and the other is Dorothy Morrison, who has had a lot to do with the new and striking packaging program of this company.

We have a feeling that the next few years will see a tremendous expansion in the use of aerosol in this industry. This will be particularly true for perfumes, cosmetics and toilet preparations, but it will also be true, to a lesser extent, and in a more limited way, to certain drug products.

Our reason for this optimism for aerosol is based upon (1) that almost everyone of the leading cosmetic and perfume manufacturers are thinking about or experimenting and testing aerosol, (2) the truly magnificent strides that have been made in containers for aerosol, which not only offer complete protection to the public, but offer a wide range of form, color, design and utility and (3) an opinion among some of the smartest people in this trade that aerosol will expand the market and increase consumption. This opinion appears particularly prevalent among cologne manufacturers.

From a few things that we have run into lately, we suspect that there is quite a substantial market for fragrance building up that is completely new to the industry. This market is what might be called the industrial use of perfume as a gift, a door opener, as advertising, or as customer good will.

For instance, we understand that a perfume manufacturer has designed a very attractive little package in which the paper box is formed something like a sleeved match box, containing a dram bottle of cologne. This little package, which looks cute, and is really nice, is produced at a cost of six cents and is sold to a major insurance company for 15c. We understand that several hundred thousand packages have been ordered by this insurance company as a door opener and a good will gift to be used by their hundred thousand agents.

Another perfume company has a rather more sumptuous package which costs 12c and which they sell for 25c to hotels and restaurants. This company has been approached by a leading automobile manufacturer with a very unique promotion plan.

When you figure what an attractive present can be made out of a perfume package at a relatively small price, it is a wonder that this use has not been expanded by business.

Outside of the notable example in our industry, that is Avon, there are in the house-to-house field many companies selling books, vacuum cleaners, brushes, etc., with far more than a million sales representatives. The same might be said of the insurance business, and in fact, in many fields of personal selling dealing with the consumer.

At any rate, some big company believes that a pleasant, inexpensive little gift by their salesman will work wonders in building a good feeling and helping to build remembrance for the company and the salesman. We think perfume fits into that category perfectly.

New Lipsticks

We are always glad to welcome anyone new to the cosmetic industry but there have been times when we have had trouble in restraining our curiosity as to the way in which some of these folks arrived in our industry.

In the case of a new comer, the path, though devious, seems to be clear. Bill Gage is the owner of Magikist Rug Cleaner, which has jumped into about a million dollar business in about ten years. According to Mr. Gage, he first brought out the lipstick as a promotion for his rug cleaning cleaning business. This was chiefly because he decided that people are much more interested in TV commercials for lipsticks than they are for rugs, which are not cleaned oftener than once a year. Since Mr. Gage found that he could sell lipsticks as well as rug cleaners, it seemed a perfectly logical conclusion to extend the Magikist trademark to a lipstick division as well as a rug division.

Modern closures should attract as well as protect

So we make sure the closure you select does both jobs well

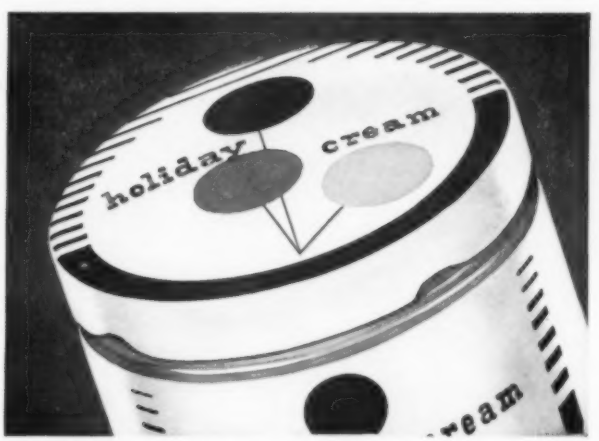
In seconds your product has to attract the customer—has to provide the information wanted—quantity, price, sales points. Your Owens-Illinois Closure can help perform this marketing function. At the same time it gives your product utmost protection—utmost convenience in use.

Careful cap design by specialists gives you a closure with sales appeal and easy readability.

Your product is protected—safe from evaporation—safe from contamination. The Owens-Illinois Tacseal innerliner seals tight—is tamperproof.

A good closure must seal well, yet be easy to remove and replace. This Owens-Illinois torque tester tells how much pressure is necessary for good sealing and easy removal.

BEFORE. Here the closure provides protection but lacks that extra showmanship needed to make quick sales at the point of purchase.



AFTER. The desired result—an attractive closure that adds to the appearance of your product—protects and does a selling job.

METAL AND PLASTIC CLOSURES
AN (O) PRODUCT

OWENS-ILLINOIS
GENERAL OFFICES · TOLEDO 1, OHIO

Debossed Designs on Caps

Armstrong Cork Company has developed a new molding process by which debossed designs can be formed in the sides of plastic caps. Prior to this development, the use of decorations on the skirts of plastic caps has been limited to a vertical direction because of technical difficulties. Designs once thought impossible, such as names, trademarks, figures, floral designs, or surfaces like wood and leather, can be debossed in perfect detail. It is also possible to "wipe" color into the etched parts of the designs to create striking effects.

A revolutionary cavity-making concept, using an electroplating process similar to that used in the manufacture of chrome parts or copper bottom kitchenware, has been perfected to produce molds with embossed designs along its walls. The problem in manufacturing plastic caps with debossed decorations on the skirt has always been to make a satisfactory mold and then to perfect a technique for removing the cap from the mold.

Sun Promotion: "Tube of Month"

The Sun Tube Corporation, Hillside, N. J., is currently employing a "Tube of the Month" promotion program, which not only demonstrates the versatility of the company's tubes but also helps publicize the products of its customers.

Each month, Sun sends to five hundred of its customers and potential customers a box containing one of the products packaged in Sun tubes, and labelled "the Sun Tube of the Month." Each box contains a card which reads: "This is one of a series of outstanding examples of better packaging in quality tubes by Sun."

Devised by Sun's president, Kenneth M. Leghorn, the "Tube of the Month" product is selected on a seasonal basis. For example the March selection was Chap-Ans, a hand cream, protective against March winds.

S. S. S. Neurabalm

The S.S.S. Company, Atlanta, makers of Three-S Tonic, tablets and Mother's Friend, has introduced a new liniment-antiseptic, Neurabalm, recommended for athlete's foot; muscular aches and pains; tired, aching, burning feet; minor cuts, minor burns; sunburn; insect bites and poison ivy. The product is packaged in four ounce bottles.

Imco Promotes Vosburgh, Simmons

Richard V. Vosburgh has been made executive vice president of Imco Container Corporation and Lee H. Simmons, a vice president, according to William K. Archer, president. Mr. Vosburgh will continue to supervise Imco's world-wide sales activities, and Mr. Simmons will continue to manage sales operations in the Eastern U. S.

New J. & J. Antiseptic

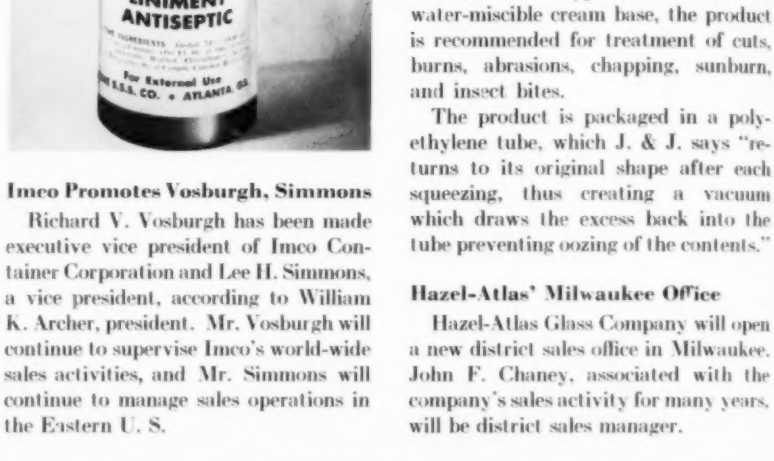
Johnson & Johnson are introducing a First Aid Cream, which is an antiseptic, as well as having an anesthetic effect, to be used in place of tincture of iodine and similar preparations. Containing bithionol (antiseptic), benzyl alcohol (anesthetic), and eucalyptol, all blended in a water-miscible cream base, the product is recommended for treatment of cuts, burns, abrasions, chapping, sunburn, and insect bites.

The product is packaged in a polyethylene tube, which J. & J. says "returns to its original shape after each squeezing, thus creating a vacuum which draws the excess back into the tube preventing oozing of the contents."

Hazel-Atlas' Milwaukee Office

Hazel-Atlas Glass Company will open a new district sales office in Milwaukee. John F. Chaney, associated with the company's sales activity for many years, will be district sales manager.

Selecting the next "Tube of the Month" to be sent to customers and potential customers of the Sun Tube Corporation, Hillside, N. J., are, left to right, Paul Curtis, sales manager of the collapsible tube division, Kenneth M. Leghorn, president, and Joseph Martin, executive vice president.



A distinctive new four-color package is now being used for Imra depilatory of Union Pharmaceutical Co., shown here in new display container.

Crown Cork & Seal Appointments

Robert J. Siebert has been appointed Northeast area sales manager of Crown Cork & Seal Company, Inc., according to John H. Scherer, can division manager of sales. Mr. Siebert will make his headquarters at "H" and Erie Avenue, Philadelphia.

Charles M. McKenna has been appointed office manager of the New York sales office, according to Mr. Siebert. The assignment of Robert Shick to the Philadelphia district sales force has been announced by George P. O'Brien, Philadelphia district sales manager of the can division.

Gair Appoints Ayers, Brakewood

Lew R. Ayers and Harold E. Brakewood have been appointed directors of product control for two folding carton division plants of Robert Gair Company, Inc., Norman F. Greenway, senior vice president in charge of folding carton operation, has announced.

Mr. Ayers will coordinate quality and product control activities at the Gair cartons division, Piermont, N. Y., and Mr. Brakewood will have the same responsibilities at the Elkhart (Ind.) plant of the ACM division.

Plume & Atwood Sales Conference

Salesmen of the fabricating division of the Plume & Atwood Manufacturing Company, Thomaston, Conn., heard R. V. Bennett, general sales manager of the division, outline the company's sales campaign when they gathered March 22 at the White Fence Inn, Thomaston, for their annual conference. They were welcomed to the meeting by I. S. Boak, president of the company. Size-for-size, the company's plant was the worst hit in the flood of August 19, 1955.

The salesmen also heard talks by Arthur Wallack, sales office manager, G E. Langeler, advertising agency president, and C. E. Boak, fabricating division manager.

Lamson Merriman Scovill of Scovill Manufacturing Co., and his bride, the former Ann Brewster Maule, are seen in Nassau, B.W.I. The couple were married February 17.

Re-elect Folding Box Assn. Head

Norman F. Greenway, vice president of the Robert Gair Company, was re-elected president of the Folding Paper Box Association of America at the annaul convention held recently in San Francisco.

Move Anchor Hocking S.F. Offices

Anchor Hocking Glass Corporation's Pacific Coast closure and tableware divisions, and its subsidiary, Maywood Glass Co., have moved their Northern California sales offices from 245 California Street to 340 Market Street, San Francisco 11.

A gleaming, heart-shaped bottle is used by Roger & Gallet for its 8 ounce bottle of a new product, Cologne Shower which comes in four fragrances. Arty black and white labeling and a slim white cap are used.

Promoted by National Can Corp.

S. M. Hopkins has been elected vice president of National Can Corporation, Robert S. Solinsky, president, has announced. Mr. Hopkins is also presently general manager of the Pacific sales division and assistant to the president. Burk Kraleman has been appointed general manager of the central sales division, according to Mr. Solinsky.

In another statement, Mr. Solinsky announced that National will shortly open a new plant for lithographing, coating and lacquering tin plate, to be located at 1961 North Cornell Avenue, Melrose Park, Ill., a suburb of Chicago.

Harry J. Flinn, one of the pioneers in the introduction of plastic bottle and jar caps for American cosmetic products, receives a desk clock-barometer from fellow employees in honor of his 50th anniversary of service with the Armstrong Cork Company. Presenting gift is R. J. Fitzgerald, manager of Armstrong's New York glass and closure office. At left is R. A. Horning, assistant general manager of the glass and closure division, who was principal speaker at the affair.
Other company officials paying tribute to Mr. Flinn included Joseph C. Feagley, vice president and general manager of the glass and closure division, and R. H. Hetzel, the division's general sales manager.

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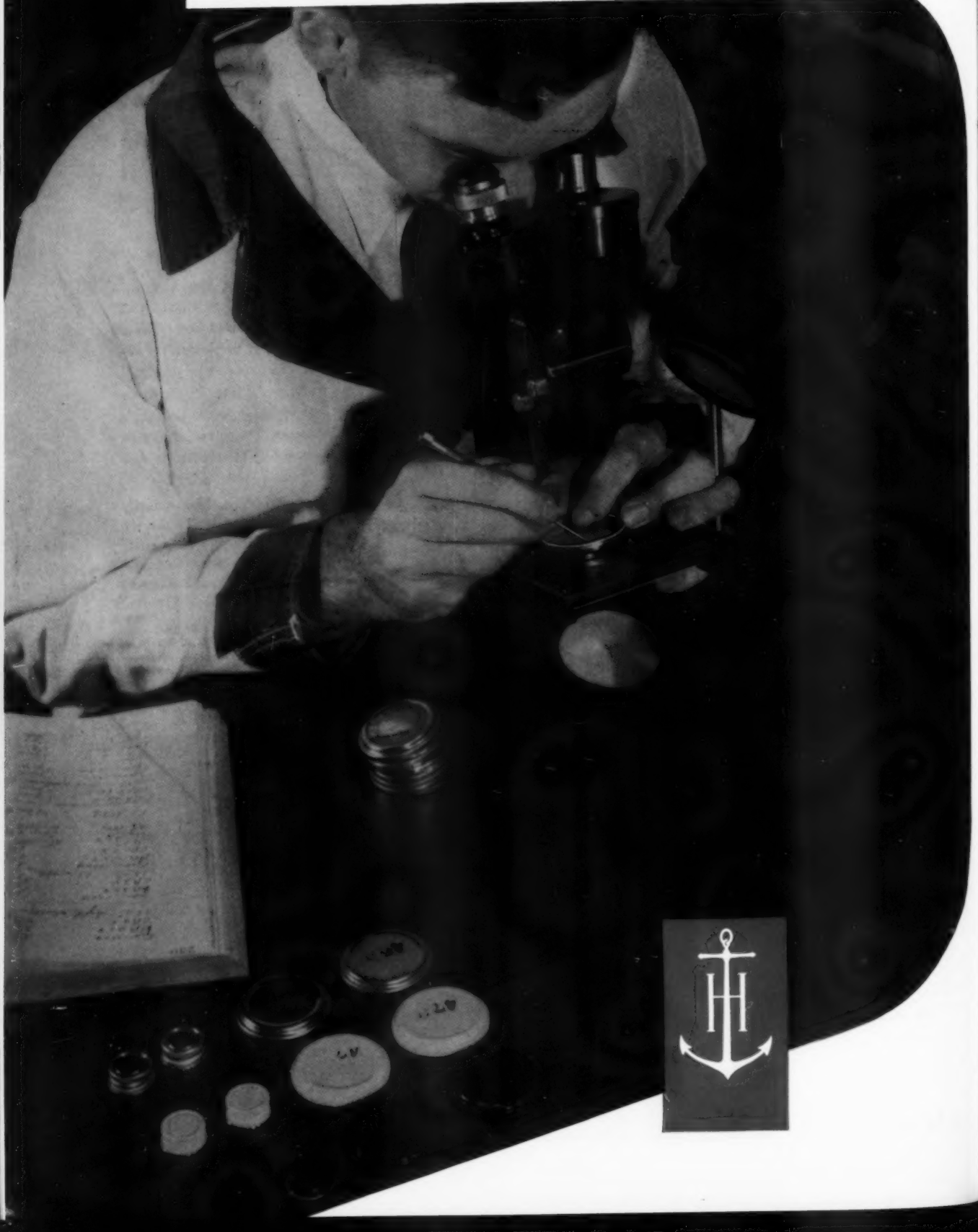

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Patent THOUGHTS AND TRENDS

by Thomas Cifelli, Jr.
PATENT ATTORNEY*

Summary of Subjects Dealt with in This Article

Recent patents dealing with antiperspirants, permanent waving solutions, antiseptics, and soap have been singled out for attention this month.

Antiperspirants

Two patents in this field, U. S. 2,734,847, issued to Carter Products, Inc., and U. S. 2,736,683, issued to Colgate-Palmolive, are thought to be of general interest.

The Carter Products patent involves the use of zirconium salts as buffers in aluminum sulfate or aluminum chloride-containing antiperspirants. According to the patent, compositions which contain the zirconium buffers are more effective as antiperspirants than known buffered preparations, and at the same time are non-irritating to the skin and non-injurious to fabrics.

The zirconium salts which are recommended are the relatively soluble zirconium salts of hydroxy aliphatic carboxylic acids, such as sodium zirconium lactate and sodium zirconium gluconate.

The amounts of the aluminum salts and the zirconium salts can be varied over wide limits, the patent states. For example, when combining aluminum chloride or aluminum sulfate with sodium zirconium lactate, the proportions may range from about 90 per cent of the aluminum salt with about 10 per cent of the zirconium salt to less than 10 per cent of the aluminum salt with over 90 per cent of the zirconium salt.

The composition may be prepared in the form of solutions, emulsions, lotions, creams and the like, which include an aqueous carrier.

The Colgate-Palmolive patent, U. S. 2,736,683, deals with antiperspirant liquids comprising aluminum sulfamate in an aqueous alcohol solution, particularly suitable for use in the form of a spray.

It is said that the resulting composition has superior antiperspirant activity, substantial non-corrosiveness to clothing fabrics, effective penetration and fast drying of the sprayed film after application usually accompanied with a mild cooling effect.

According to the patent, actual perspiration-lessening effects were determined by tests and these show that aluminum sulfamate was from three to six or more times effective as aluminum sulfate of comparable concentrations. It is also stated in the patent that no corrosion-inhibiting agents are required with aluminum sulfamate as this ingredient is relatively non-corrosive on fabrics.

As is generally true in connection with these compositions, the proportion of aluminum sulfamate antiperspirant may be varied over wide limits. The patent says that satisfactory results can be obtained where the quantity of aluminum sulfamate incorporated ranges from about five per cent up to about 50 per cent by weight of the total preparation, and that a preferred range lies between about 10 per cent to 30 per cent by weight.

The Colgate inventors frankly disclose that under certain severe conditions where aluminum sulfamate is improperly applied to clothing and is not removed by previous washing or cleaning there may result some discoloration of cellulosic fibers upon ironing, pressing, or the like:

> "The discoloration appears as yellowish to brown cast when applied to and dried by heat on white fabrics made of cotton, linen, or regenerated cellulosic fibers. This discoloration tendency can be prevented or satisfactorily lessened by incorporation in the antiperspirant preparation certain organic compounds which should be soluble in aqueous alcoholic aluminum sulfamate and which does not precipitate therefrom a compound containing aluminum."

These discoloration inhibitors include certain amides, amino carboxylic acids, salts of non-hydroxy saturated carboxylic acids and ammonia bases and compounds which contain the functional group:

$$\equiv C - S - H$$

In order to obtain more effective penetration the use of surface-active materials is recommended, in amounts up to about one per cent by weight.

The liquid antiperspirants may be employed either with or without the alcohol in an aerosol type dispenser under pressure in combination if desired with a propellant or liquefied normally gaseous substance. Propellants such as the "Genetrons" and "Freons" are particularly suitable.

Permanent Waving Solution

There were two recent patents dealing with this subject. U. S. 2,736,323 was issued to Everett G. McDonough and assigned to Tide Water Patent Development Company. U. S. 2,738,304 was issued to W. S. Arnold and assigned to The Gillette Company.

The McDonough patent is a continuation-in-part of the well-known patent U. S. 2,577,710, which has been involved in litigation.

Perhaps as good an idea as any concerning the subject matter of this patent will be gleaned from claim 3 of the patent. The claim is set forth below:

> "A permanent waving composition comprising a mercaptan selected from a group consisting of mercapto-acetic acid, mercapto-propionic acid, mercapto-butyric acid, and mercapto-caproic acid, in a solution containing an alkaline material having a dissociation constant less than 5×10^{-3}, said solution having a pH ranging from about 9.2 to not higher than 9.5, the concentration of said mercaptan in terms of weight per volume ranging from about two per cent to about 10 per cent, the concentration of mercaptan and the pH of the solution being adjusted within said ranges to obtain a permanent change in the configuration of human hair during a given time of application without damage to the hair structure by having the concentration of mercaptan in the higher portion of said concentration range for a lower pH and having the concentration of mercaptan in the lower portion of said concentration range for a higher pH within the stated pH range."

*Richards and Cifelli
Newark, New Jersey

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A new molding process, pioneered by Armstrong, reproduces almost any debossed decoration on the skirt of your molded cap. Names, trademarks, figures, and floral designs are just a few of the possibilities. Surfaces like cloth, wood, and leather can be simulated, too. You get perfect detail, as in the sharp lines of the striking, star-spangled cap shown above.

Let this Armstrong-pioneered process bring new beauty to your package. Call your Armstrong man today or write Armstrong Cork Co., Glass and Closure Division, 5303 Chester Street, Lancaster, Pennsylvania.

Armstrong MOLDED CAPS

The Gillette patent, U. S. 2,738,304, deals essentially with a creaming composition for use in aqueous cosmetic preparations, especially hair waving solutions.

The patent points out that there is a tendency for hair waving solutions which include opacifiers to separate out on standing. This results in an unsightly appearance. Another disadvantage of such opacifiers resides in the fact that they tend to plug the capillaries of filling and thereby greatly complicate the filling operation.

The Gillette patent provides a creaming agent or opacifier which does not have either of these faults and which is fully compatible with components normally found in cold wave lotions. In the words of the patent:

"Generally described, the composition herein comprises a mineral oil, a sulfonated vegetable oil and an ester of an aliphatic di- or trihydroxy alcohol, as ethylene glycol, propylene alcohol, glycerol, etc., and a high molecular fatty aliphatic acid, e.g., lauric, stearic, oleic, palmitic and the like. Additionally, the composition generally comprises lanolin or a lanolin derivative such as 'lanogene,' which is described as a mixture of the more volatile constituents of lanolin."

Claim 1, set out below, gives an idea of the actual composition:

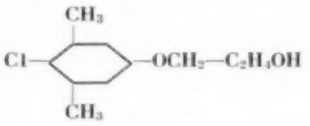
"A composition adapted for use as a creaming agent in aqueous alkaline cosmetic preparations, which includes a mineral oil having a Saybolt viscosity at 100° F. of from about 50-150 seconds, an ester of a fatty acid having a molecular weight at least as high as lauric acid and an alcohol from the class consisting of di- and tri-hydroxy alcohols, a sulfonated vegetable oil and up to about 30 per cent of lanolin, said composition in the respect of the mineral oil, sulfonated vegetable oil, and ester conforming to the limits below:

	Percent
Mineral oil	59-80
Sulfonated vegetable oil	2.5-15
Ester	6-26."

Antiseptics

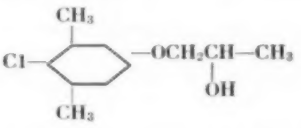
Here too there have been two recent patents thought to be of general interest. U. S. 2,734,087, issued to Carter Products Inc., and U. S. 2,735,872, issued to Monsanto are the patents referred to.

The Carter Products patent covers new fungicidal and bactericidal agents. These are the hydroxy-n-n-propyl ethers of p-chloro-m-xylenol and have the general formula



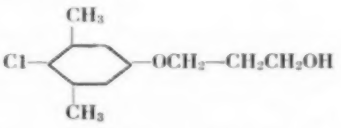
Specific compounds of this general type and their physical properties are as follows:

1 - (3,5 - dimethyl - 4 - chlorophenoxy)-2-propanol,



This compound is a white crystalline solid, melting point 62° C., less than 0.1 per cent soluble in water at ordinary room temperature, and soluble in most common organic solvents.

1 - (3,5 - dimethyl - 4 - chlorophenoxy)-3-propanol,



This compound is a white crystalline solid, melting point 53-54° C., less than 0.1 per cent soluble in water at ordinary room temperature, and soluble in most common organic solvents.

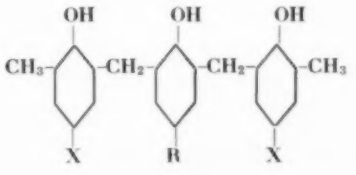
These compounds may be prepared by a variety of methods, the most convenient of which are the following:

1. Condensation of 3,5-dimethyl-4-chlorophenol (also known as p-chloro-m-xylenol) with the appropriate chlorohydrin, using alkali in aqueous or non-aqueous solution as the condensing agent.

2. Condensation of 3,5-dimethyl-4-chlorophenol with the appropriate epoxide, using alkali as the condensation catalyst.

The Monsanto patent, U.S. 2,735,872, deals with new tris-phenols which are said to be particularly useful in detergent soap compositions.

The tris-phenols have the general formula:



where X is a halogen atom and where R is a long chain alkyl radical such as a nonyl radical.

The new compounds are said to be readily incorporated in liquid or solid detergent soaps. Relatively small amounts are said to be required in order to yield effective antiseptic detergents. Amounts from one to three per cent by weight upon the detergent soap are preferred but amounts from ½ to 10 per cent by weight may be employed.

Solid Potassium Soaps

A patent which appears to mark a large step forward in the soap industry was recently issued to Armour and Company. This patent, U. S. 2,738,335, discloses a method for producing solid potassium soap.

The solid potassium soaps of this invention are said to possess a number of advantages over the conventional solid sodium soaps. One of these is that when dirt is removed from a surface by the action of a potassium soap it is much less likely to be redeposited on the surface than when sodium soap is used. Another advantage of potassium soap is that it can be used to a high degree of effectiveness in sea water, as compared to sodium soaps. Furthermore, solid potassium soaps made exclusively from the fatty acids of tallow do not suffer from the same disadvantages as sodium soaps prepared exclusively from tallow. It is therefore unnecessary to employ somewhat expensive coconut oil fatty acids to produce a good solid potassium soap. Potassium soaps prepared exclusively from tallow fatty acids are less irritating to the skin, since coconut oil fatty acids tend to be more irritating than tallow fatty acids; all this the patent states. A somewhat purely nationalistic advantage of the potassium soaps prepared without the use of coconut oil fatty acids is that production of good soaps is thereby rendered independent of imported raw materials, such as coconut oil.

The patent points out that at the present time commercial solid soap products are mainly sodium soaps. In fact, nearly all solid soaps, and in particular solid soaps in the form of bars and granules, are composed entirely of sodium soaps. However, in the case o solid soap in the form of flakes, it is the general practice, especially in the case

(Continued on page 552)

NEW PERFECTION
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UNIFORMITY	A-1
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#1

Non-rolling, extra-depth, Bakelite cap; thick-flange rubber bulb; Saftee-ball glass.

#3

Regular plastic cap; thin flange rubber bulb; semi-blunt glass.

#4

Metal cap: AMEKINE oil-resisting synthetic rubber bulb; blunt glass.

They're A-1 with your customers, too . . . assuring you repeat sales!

When you sell a product that pleases and satisfies your customers, you're assuring yourself of their goodwill and continued patronage. New Perfection Dropping Parts help to give you that kind of a product. They are convenient, attractive, dependable—manufactured and assembled under careful and constant inspection to assure the highest possible quality.

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CAPS of plastic or metal can be furnished in a complete range of sizes and colors.

DROPPER GLASSES are available in a wide variety of styles and sizes; plain or CALIBRATED in any color to mark specific dosages.

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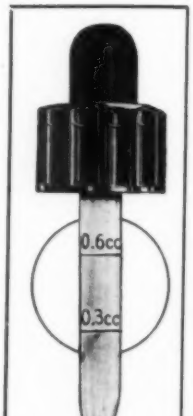
We can make up dropping parts to fit your own bottles or we can supply bottles in an attractive modernistic style in Amber, Blue, Green, or Clear glass, complete with dropping parts, in the following sizes: ⅛, ¼, ½, 1 and 2 oz.



#2

Non-rolling extra-depth Bakelite cap; thick flange rubber bulb; special bent glass. (Calibrated in color).

• • • • •

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NEWS . . .

Rhodia Is in New Offices

Rhodia, Inc. has moved into new and larger offices with improved facilities at 60 East 56th Street, New York 22. The new telephone number is PLaza 3-4850. The move permits expansion of Rhodia's Aromatics, "Alamask" and other divisions as well as more rapid handling of customers' requests and orders, said a spokesman for the company.

Heiges Elected Pfizer Secy.

Jesse G. Heiges has been elected secretary and general counsel of Chas. Pfizer & Co., Inc. A member of the company's legal staff since 1950, Mr. Heiges has been assistant secretary for the past four years. Formerly associated with the New York law firm of Mudge, Stern, Williams and Tucker, he served in the U. S. Navy as a submarine-chaser commanding officer in World War II.

JESSE G. HEIGES

NY Cos. Chem. Ch. Meeting

Dr. Ernest Guenther, vice president and technical director of Fritzsche Brothers, Inc. and a 1955 recipient of the Cosmetic Chemists Award, will be the featured speaker at the Brass Rail Restaurant, New York, on April 25, when the New York Chapter of the Society of Cosmetic Chemists will hold its Ladies' Night. Dinner will be served at 6:30 P.M.

Dr. Guenther will present a "World Wide Travelog" with motion pictures and slides. Each woman attending will receive a gift-package.

Dr. D. H. Powers to Speak

Dr. Donald H. Powers, director of cosmetic research at Warner-Lambert Pharmaceutical Company, will speak on "Recent Developments in the Field of Cosmetics" at the Annual Ladies' Night Dinner-Meeting of the Raritan Valley Subsection of the North Jersey Section of the American Chemical Society. The meeting will be held April 18 at the Johnson & Johnson Research Center, New Brunswick, N. J. The buffet dinner will start at 6:30 P.M.

Old Empire Comptroller

William F. Meyers has been appointed comptroller of Old Empire, Inc., Newark, N. J., according to John de Elorza, executive vice president of the firm. Mr. Meyers was formerly comptroller of the Chase Chemical Co. of Newark.

Lederle Labs' Sales Director

Harry W. McNey has been appointed director of sales for the Lederle Laboratories division of the American Cyanamid Company, L. C. Duncan, general manager, has announced. Mr. McNey assumed his new post April 1, replacing Henry Wendt Jr., who has been made vice president and general manager of Cynamid's Davis & Geck division.

HARRY W. McNEY

Penick Forms French Firm

S. B. Penick & Company has announced the formation of S. B. Penick & Company (S.A.R.L.) with headquarters in Chatou, France. The managing director is Henri Beaudichon, Penick's representative in France since 1946. The French firm complements Penick's association with C. F. Gerhardt Ltd. of London.

Endo's New Corporate Name

Endo Products Inc. is changing its corporate name to Endo Laboratories Inc., according to an announcement by Joseph Ushkow, president.

Ivan Budd Anniversary

Many, many years ago, a bright, pink-cheeked, curly haired (it's a fact) young lad came to New York from the hills of Ithaca, New York, with a chemistry diploma in his hand. Almost before he knew it, he was in the essential oil business.

It was among the vats and the stills in the factory of Antoine Chiris that Ivan Budd first acquired that twitching nose which can detect an aromatic element no matter how it is disguised. It was during this period, also, that he first developed that urge to leave the cloister of the factory and the laboratory for the perils of the life of a salesman.

This urge to sell led Budd from Chiris to Julian Lyon, then an essential oil house, from there to the purchase of this company and the formation of his own company, Wangler-Budd and finally to a merger of this company with Ungerer & Co.

Just recently Ivan Budd, with appropriate ceremonies, celebrated his first twenty years with Ungerer & Co., as vice president and company director. Many friends including customers, competitors and casual standers-by wish Buddy as vigorous and happy another twenty years as those just passed.

IVAN BUDD

Life Products Marketing Div.

John L. Shirley has been appointed director of marketing for Life Products International, Chicago. He was formerly assistant general sales manager of J. B. Roerig & Co. Mr. Shirley is also connected with Illinois Bio Co. of America and Bio-America Co. He is concerned with the marketing of Wey-Rite, a completely balanced food alternate, through Life Products International, and similarly with Bevemino, a therapeutic balanced food alternate, through Bio-America, distributor for this product to the medical profession.

THE POPULAR

is NOW AVAILABLE IN
A LARGER SIZE
because you asked for it!!!

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TOUCH-N-FLO*
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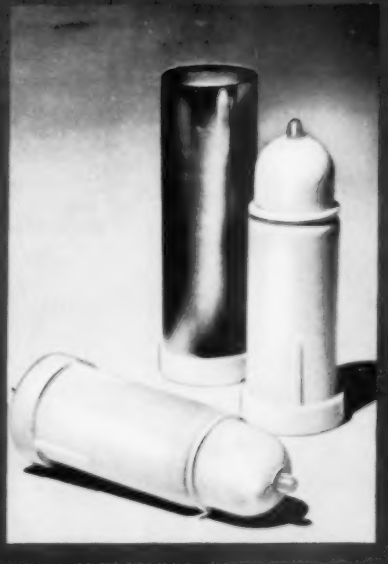
* U. S. PATENT

the 18 mm. TOUCH-N-FLO with our new Victoria Bottle.



So dramatically successful in its small plastic container style with gold-metal cap.

And so practical in a glass bottle with slip-on brass cap version.

the NEW 18 mm. TOUCH-N-FLO fits *any* Bottle *with* 18/410 *Neck. Write now for samples and prices.*

Touch-n-Flo is ideal for cream perfumes or cream sachets, powder, liquid soaps, lotions, and deodordants — contents always flow with a touch, yet never leak.

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With the panel in the background, those attending the American Society of Perfumers' Second Annual Symposium on Fragrance take time out from the discussion of methods for pre-determining consumer acceptance of new fragrances to do an about-face for the photographer.

Fragrance Symposium Held

In pre-market testing of new fragrances, the perfume industry will begin to draw more heavily on the knowledge of psychology and other sciences concerned with human motivation, according to the tenor of discussion at the Second Annual Symposium on Fragrance.

Sponsored by the American Society of Perfumers, the symposium was held March 21 in New York's Essex House, where representatives of leading fragrance and toiletries firms joined with experts in marketing research and other fields for an interchange of ideas on the principles underlying consumer acceptance.

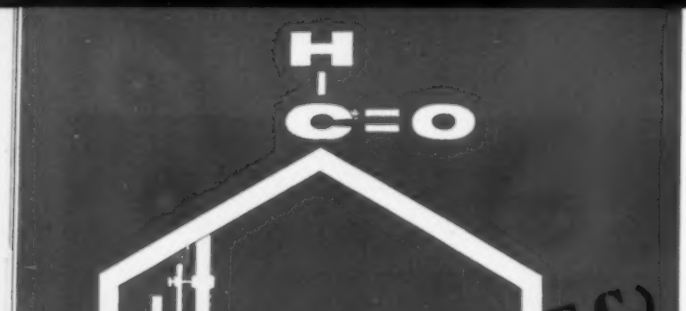
Subjects discussed by the symposium panel were concerned with pre-market testing and other aspects of consumer acceptance of fragrance. Moderator was Frazer V. Sinclair, publisher of Beauty Fashion magazine and Drug and Cosmetic Industry. The society awarded honorary membership to William A. Poucher, perfumer for Yardley of London, in recognition of his contributions to the perfume industry in research and new products.

Members of the panel and their topics were:

"A Perfume Is Born, Pierre L. Bouillette, Givaudan - Delawanna; "What Fragrance Means to Women," Mrs. Miriam Gibson French, beauty editor, McCalls Magazine; "Perfume, the Big Gamble," Jack Mohr, general manager of Lentheric, Inc.; "Use of the Non-expert Panel for Testing Cosmetic Fragrance," Dr. Donald H. Powers, director of cosmetic research, Warner-Lambert Pharmaceutical Co., Inc.; "Laboratory Pretesting of Cosmetic and Fragrance Products," Dr. Dean Foster, director of laboratories, United States Testing Company; "A Case History in Fragrance Testing and Evaluation," John R. Carr, product manager, Revlon Products Corporation.

"The Role of Olfaction in Personality," Marvin Stein, M.D., Hospital of the University of Pennsylvania; "An Olfactory Aptitude Test for the Selection of a Perfume Panel," Gustav Carsch, chief perfumer, The Toni Company; "Perfume and Human Motivations," Irving Gilman, vice president, Institute for Motivational Research; "Measuring the Effect of Perfume upon Product Acceptability," Miss Eleanor K. Coen, consumer research manager, Lever Brothers Company; "Monadic Type Product Test,"Henry Brenner, president, Home Testing Institute; "Psychological Oddities of Perfume and Fragrance," Jean Millon, sales manager, Coty Incorporated.

Pride and pleasure can be read in the broad smile of William Lackey, Squibb sales representative, whose tie is being adjusted by J. C. Leppart, executive vice president of Olin Mathieson Chemical Corporation. The two exchanged ties in award ceremonies held recently in New York honoring Mr. Lackey as the top Squibb salesman in the U. S. during 1955. The blue vase being held by W. L. Arscott, Squibb sales vice president, as J. J. Toohy, general manager of Squibb, fills it with champagne, is symbolic of Squibb sales supremacy.



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The Heyden sales office nearest you will welcome the opportunity to discuss your requirements, or see that you receive samples and technical information.

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p-Chlorobenzaldehyde
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p-Chlorobenzoic Acid
2,4-Dichlorobenzoic Acid
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Congressmen Visit Lilly

Thirteen members of the House Interstate and Foreign Commerce Committee, accepting an invitation by Eli Lilly and Company's president, Eugene N. Beesley, were conducted on a two-day inspection tour of the company's polio vaccine and antibiotics manufacturing facilities in Indianapolis. The congressmen expressed satisfaction with the manufacturer's role in making and testing the vaccine.

Headed by Chairman J. Percy Priest (D., Tenn.), the visiting committee members included Representatives Samuel N. Friedel (D., Md.), Oren Harris (D., Ark.), Joseph P. O'Hara (R., Minn.), Walter Rogers (D., Tex.), James I. Dolliver (R., Ia.), John W. Heselton (R., Mass.), Don Hayworth (D., Mich.), John V. Beamer (R., Ind.), William L. Springer (R., Ill), Paul F. Schenck (R., O.), Joseph L. Carrigg (R., Pa.), and Steven B. Derounian (R., N. Y.).

Accompanying the committee on its tour was Dr. Leonard A. Scheele, Surgeon General of the United States Public Health Service, and Congressman Charles B. Brownson of Indiana's Eleventh District, in which Lilly's two Indianapolis plants are situated.

Dr. Thomas P. Carney, Lilly's vice president for research, development, and control, told the committee about research trends. Dr. Clyde G. Culbertson, director of the biological research division, discussed polio vaccine testing methods.

Congressmen became "men in white" when thirteen members of the House Interstate and Foreign Commerce Committee donned laboratory caps and gowns during a February 23 and 24 tour of Eli Lilly and Company's polio vaccine plant in Indianapolis. Dr. H. A. Dettwiler, director of Lilly's biological production division, holds a bottle to explain how virus is grown on a culture of kidney cells in the incubation room. The attentive legislators are, left to right, Joseph P. O'Hara (R., Minn.), J. Percy Priest (D., Tenn.), chairman of the committee, and Oren Harris (D., Ark.).

Evans Library Staffers

Dr. Eric J. Hewitt, vice president of Evans Research and Development Corporation, has announced the appointment of a full-time library staff of two: Mrs. Rosalie Morris, librarian, and Miss Ellen Fisher, library clerk.

Swiss Co. Exec. Tours Ultra

In the U. S. for a year's tour of soap and chemical plants, George Strauli, plant manager of Strauli & Co., Winterthur, Switzerland, recently visited the Ultra Chemical Works, Inc., Patterson, N. J., an associate of Witco Chemical Company.

An Ultra customer, Strauli & Co. is one of the oldest soap-making firms in Switzerland.

Supervising B-M Sales Div.

Harry Hessen has been appointed division supervisor of the Eastern sales division of Bristol-Myers Products Division, according to an announcement by E. Lloyd Bernegger, vice president in charge of sales.

Yonkman Receives Two Scrolls

Dr. Fredrick F. Yonkman, vice president in charge of research for Ciba Pharmaceutical Products, Inc., received two scrolls March 8 in Detroit at the testimonial luncheon of the tenth annual Michigan Clinical Institute.

The Michigan State Medical Society presented a scroll to him as "official representative of the pharmaceutical industry at the 1956 Michigan Clinical Institute in deep appreciation and grateful recognition of distinguished service rendered to the peoples of the world through scientific research, modern production and distribution of life-saving drugs and education of the public in the great advances of medicine."

A second scroll was presented to Dr. Yonkman by the Michigan State Pharmaceutical Association "in acknowledgment and commendation of this valuable community service and leadership for the benefit of his fellowmen."

McNeil Labs Founder Retires

Robert Lincoln McNeil, founder of McNeil Laboratories, Inc., Philadelphia, has announced his retirement as president. He will continue with the firm as consultant and director.

Robert L. McNeil Jr. has been elected to the newly created senior office of chairman of the board; Henry S. McNeil has been elected president and James A. Noone, vice president and treasurer.

ROBERT L. McNEIL, JR.

HENRY S. McNEIL

Elect Two to van A-H Board

Mrs. William T. Haebler and Henry G. Walter Jr. were elected to the board of directors of van Ameringen-Haebler at a special meeting held February 29, according to an announcement by A. L. van Ameringen, chairman.

Mrs. Haebler is a director of the Kurth Malting Co., Inc., of Milwaukee. Mr. Walter, a partner in the law firm of Fulton, Walter and Halley, is director of the Heyden Chemical Co. and the St. Maurice Chemical Co., Ltd., of Canada.

DR. HARRY J. ROBINSON

DR. KARL H. BEYER

Witco Oil, Gas Wells Sold

Witco Chemical Company has sold all of its 25 oil and gas wells, according to an announcement by R. I. Wishnick, board chairman. Fifteen of the wells were sold to Producing Properties, Inc., Dallas, for approximately $1,750,000.

"Proceeds of this sale," said Mr. Wichnick, "will be used in a long-range chemical expansion program. Our decision to dispose of all the oil and gas properties was made because they did not logically fit in with our plans for continued growth and expansion in the chemical field."

Merck Inst. Staff Doubled

By shifting control of several research groups at West Point, Pa., from its Sharp & Dohme Division to its Institute for Therapeutic Research, Merck & Co., Inc. has approximately doubled the facilities and staff of the institute. Formerly vice president and director of research of Sharp & Dohme, Dr. L. Earle Arnow has been elected executive director of the institute. He is also vice president of the Sharp & Dohme Research Laboratories Division.

Director of the institute since its founding in 1933, Dr. Hans Molitor has been appointed director of scientific relations of Sharp & Dohme Research Laboratories, and he has been elected chairman of the institute's board of trustees, succeeding George W. Merck who resigned.

Dr. Harry J. Robinson, former associate director of the institute, has been appointed director of its Rahway, N. J. unit, and Dr. Karl H. Beyer, former head of pharmacological research at Sharp & Dohme, has been appointed director of the institute's West Point unit.

Sterling Quarto-centenarians

Forty-five employees of the domestic divisions and subsidiaries of Sterling Drug Inc. were admitted to membership in the company's Quarter-Century Club March 16 in a ceremony held at the Roosevelt Hotel, New York. This brings the club's total membership to 471, of which 330 are still active in the company. Attending the affair were eight of the 141 retired members as well as directors and officers of Sterling and its affiliates.

DR. L. EARLE ARNOW

DR. HANS MOLITOR

L. Givaudan Visits NY Firms

Returning from Geneva and Paris to Brazil, Leon Givaudan, co-director of Companhia Brasileira Givaudan and son of Andre Givaudan of L. Givaudan & Cie., S.A., Geneva, spent several days in New York and visited firms directly interested in Brazilian activities of the industry.

Elected Pinkham Sec., Dir.

Hermon E. Smith Jr., sales manager of the Lydia E. Pinkham Company—and great-grandson of Lydia Pinkham—has been elected secretary and director of the company.

Hansen Heads Hilton-Davis

Election of Harold L. Hansen, Ph.D., as vice president of Sterling Drug, Inc., in charge of the Hilton-Davis Chemical Co. Division, has been announced by James Hill Jr., chairman of the board. Dr. Hansen succeeds the late James F. Thompson.

Associated with Sterling for 14 years, Dr. Hansen has been chairman of its quality control committee since 1947. He also was director of control for Winthrop Laboratories' plants. Dr. Hansen received his Ph.D. in organic chemistry and pharmacology in 1932 from Northwestern University, where he taught chemistry from 1929 to 1938.

Grongoire Expands Plant

Grongoire, manufacturer of private label cosmetics, has acquired 10,000 square feet of additional space at its plant, 127 Green Street, Brooklyn, N. Y., according to an announcement by Syd Dunn, president. Equipment has been installed, and the firm has increased production and service facilities.

Gross Joins Abbott Labs

Formerly head of pharmaceutical research for Commercial Solvents Corporation, Herbert M. Gross, Ph.D., has joined the pharmaceutical research department of Abbott Laboratories.

C. M. DONELSON

JOHN VALIANT

C&CC Co. Div. Sales Mgrs.

R. C. Boltz and J. R. Hulten have been appointed division managers and H. P. White, assistant division manager for Carbide and Carbon Chemicals Company, a division of Union Carbide and Carbon Corporation, according to an announcement by E. E. Fogle, vice president of the company.

Former manager for the Newark, N. J. district, Mr. Boltz has been appointed Eastern division manager and will be located in the New York office. Mr. Hulten has been appointed Central division manager and will be located in Cleveland. He was formerly manager for the Philadelphia district. Mr. White, former manager for the Chicago district, has been appointed Pacific Coast assistant division manager and will be located in San Francisco.

Emulsol Installs Pilot Plant

With the installation of a pilot plant for production of polyurethane foams at the Chicago laboratories of its Emulsol Division, the Witco Chemical Company now has complete facilities for technical service on the foams. Heart of Emulsol's new installation is a specially designed proportioning-mixing machine.

Previously, technical service—and even research—on the new resin has been handicapped by lack of suitable equipment with which to duplicate forms made in large production units, according to Dr. Charles F. Fuchs, Emulsol vice president in charge of research. With polyurethane foams now being used to pad crash panels in automobiles, experiments are underway to adapt them to pillows, mattresses, upholstery and other markets.

Witco and its divisions have no intention of starting foam production, Max A. Minnig, Witco president, has pointed out. "We are interested only in the manufacture of raw materials that will improve the qualities of polyurethane foams," he said.

Dr. Edw. J. Hughes Retires

Dr. Edward J. Hughes, manager of Eli Lilly and Company's analytical department for the past twenty-five years, retired February 29. While with Lilly, he was a leading proponent of the advancement of analytical methods and techniques through the use of instrumentation.

A native of Pennsylvania, he was graduated from the Philadelphia College of Pharmacy and Science in 1916 with the degree of Doctor in Pharmacy and was awarded an honorary Master of Pharmacy degree by the college in 1938. He did graduate work in experimental organic chemistry in 1925 at the University of Pennsylvania.

After a year's military service with the United States Army in World War I as an analytical chemist on the staff of the Surgeon General in Washington, Dr. Hughes became an instructor at the Philadelphia College of Pharmacy and Science and later, assistant professor of chemistry. During his eight years on the faculty, he was associated with or taught many men who are now members of the Lilly organization.

Burroughs Wellcome Appoints

Burroughs Wellcome & Co., Inc. has announced the appointment of John Valiant to a newly created position as co-ordinator of new product development activities, in which post he will be assistant to the marketing manager.

C. M. Donelson has been appointed to a newly created position in the sales division. His duties will include recruitment and training of new representatives and the preparation of certain sales promotion material.

Curtis Diversification Post

Helene Curtis Industries, Inc. has established a corporate acquisitions department, which will be headed by Harold J. Rosen, executive assistant to the chairman of the board. The function of the new department, said Gerald Gidwitz, chairman, will be to seek corporate properties for purchase. This procedure, he said, will formalize and intensify the company's diversification program, conducted on a smaller scale for several years.

Nysco Moves to New Plant

Nysco Laboratories has announced initiation of operations at its new plant, 34-24 Vernon Boulevard, Long Island City, New York, about 15 blocks from its former location. Prior to moving the old plant, according to a spokesman, Nysco set up an entirely new plant at the new site and, in effect, now has double the capacity of the former operation.

The firm has a new department for imprinting capsules for identification. Imprinting can be done in any color, with product name on both sides of either half of capsule.

ALPHA METHYL CINNAMIC ALDEHYDE

Typical Specifications:

PHYSICAL APPEARANCE:	Light yellow liquid.
ODOR TYPE:	Cinnamon, Cassia.
SOLUBILITY:	10 parts soluble in 12 parts of 80% Ethyl Alcohol.
STABILITY:	Stable in presence of alkalies—of excellent lasting quality.
REFRACTIVE INDEX $n\frac{20}{D}$:	1.6040
SPECIFIC GRAVITY $\frac{20}{20}$:	1.036
QUALITY:	Carefully produced to rigid specifications and checked in our modern control laboratories.
SUGGESTED USES:	A notable and successful raw material for the production of OIL CASSIA SYNTHETIC.

Investigate these additional VERONA specialties:

CYCLAMAL • DIMETHYL OCTANOL SPECIAL

RESEDALIA • VERONOL • ROSANOL

Sole representative in the United States for J. & E. Sozio, Grasse, France

Resinoides **Essential Oils** **Natural Absolutes**

Write us for our complete list of specialties and other aromatic chemicals.

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PRODUCTS BUILD SALES FOR *Your* PRODUCTS

Aromatics Division

VERONA CHEMICAL COMPANY

Plant and Main Office: 26 Verona Avenue, Newark, N. J.

1210 Rosedale Avenue, Chicago, Ill.

Flavor Extract Mfrs. Conv.

Dr. Robert A. Osborne, chief of Beverage Inspection Division, Food and Drug Administration, and Dr. C. O. Willits of the U. S. Department of Agriculture, Agricultural Research Service, will be among the speakers at the 47th annual convention of the Flavoring Extract Manufacturers Association, to be held May 13 to 16 at the Hotel Traymore, Atlantic City. Dr. Willets will discuss maple research progress.

In addition to a talk on "The Vanilla Bean Market" by Ray Schlotterer of the Vanilla Bean Association and the annual report of John Hall, F.E.M.A. executive secretary and general counsel, there will be the following committee reports:

Scientific Research, Dr. A. S. Wendt; Food Additive, Harold Janovski. There will be a report on vanilla research by Dr. George McNew of the Boyce Thompson Institute, followed by a question and answer period, Dr. Edward Prill presiding, and a report on vanilla publicity by Barney Lewis. J. M. Wenneis will discuss spray-dried flavors and Dr. David Jorysch, stabilization of citrus oils and beverages.

Entertainment features of the convention include the hospitality party on Sunday, May 13, the convention luncheon, golf tournament, boat ride, and shore dinner on Monday; an association luncheon and the president's reception and dinner dance on Tuesday. The chemists' breakfast on Wednesday will be followed by a general session of the association.

Robert Krone of Fritzsche Brothers, Inc. is chairman of the convention committee, which includes Charles P. McCormick Jr., McCormick & Co.; William X. Clark, Sterwin Chemicals, Inc.; and Frank Green, National Aniline Division, Allied Chemical & Dye Corp.

Edwin L. Schneider Retires

On St. Patrick's Day, the 40th anniversary of his employment by S. B. Penick & Co., Edwin L. Schneider, assistant secretary, retired. He was the first person employed by the company in New York when the late S. Barksdale Penick Sr. moved his headquarters there from North Carolina.

Weco Exec. V.P.: Coffman

Election of Clifford B. Coffman Jr. as executive vice president of Weco Products Company has been announced by J. J. Weber, Weco president. Mr. Coffman will be in charge of merchandising and marketing planning.

Rhodia Laboratories Mgr.

Jacques P. Sibeud, Ph.D., has been appointed manager of laboratories for Rhodia, Inc. A native of Toulon, France, he received his degree from the University of Lyon in 1952, following which he joined Rhone-Poulenc, Paris, where he worked on development, control and research of synthetic aromatics. He is a member of the Societe Chimique de France.

Shulton Buys Plant in Canada

Shulton, Inc. has purchased a new plant in Toronto, Canada, according to an accouncement by George L. Schultz, president of the company. Located in the new Don Mills Model Industrial Section, the modern one-story building, occupying 32,000 square feet of the four acres purchased by Shulton, will be headquarters for all Shulton sales and manufacturing throughout the Dominion.

Shulton acquired the property to provide the more extensive manufacturing facilities needed to meet increasing demand for the firm's toiletries lines.

Architect's sketch of the new Shulton, Inc. plant in Toronto, Canada.

IRWIN S. SHUPE

Winthrop Control Director

Appointment of Irwin S. Shupe as director of control at the principal manufacturing plant of Winthrop Laboratories in Rensselaer, N. Y., has been announced by Dr. Theodore G. Klumpp, president. Formerly assistant director of control, Mr. Shupe succeeds Dr. Harold L. Hansen, who was elected a vice president of Sterling Drug Co., in charge of the Hilton-Davis Chemical Co. division, Cincinnati.

Perry Bros. Subsidiary

Perry Bros., Inc., Woodside, N. Y., has established the Perbro Laboratories division, which will manufacture essential oils and flavor bases for the pharmaceutical, beverage and food fields.

Ben Perry, vice president, has appointed two research chemists for the new division. Herbert J. Bass will be in charge of the technical service program and Allen J. Baron, quality control and production.

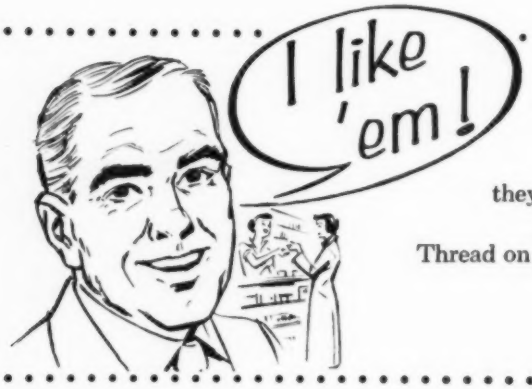
Magnus on Dispensary Board

Joseph Baird Magnus, vice president of Magnus, Mabee & Reynard, Inc., has been elected to serve on the board of managers of the North-Eastern Dispensary in the City of New York for the term ending February, 1958. The dispensary is one of the oldest charitable organizations in the borough of Manhattan.

"Seagull" Distributor

Appointment of Whittaker, Clark & Daniels, Inc. as sole distributor of Reckitt's "Seagull" Ultramarines in the United States has been announced. Available in a wide range of ultramarine shades, "Seagull" brand blues will be distributed by Whittaker, Clark & Daniels to the paint, ceramic, rubber, paper, ink, textile and other industries.

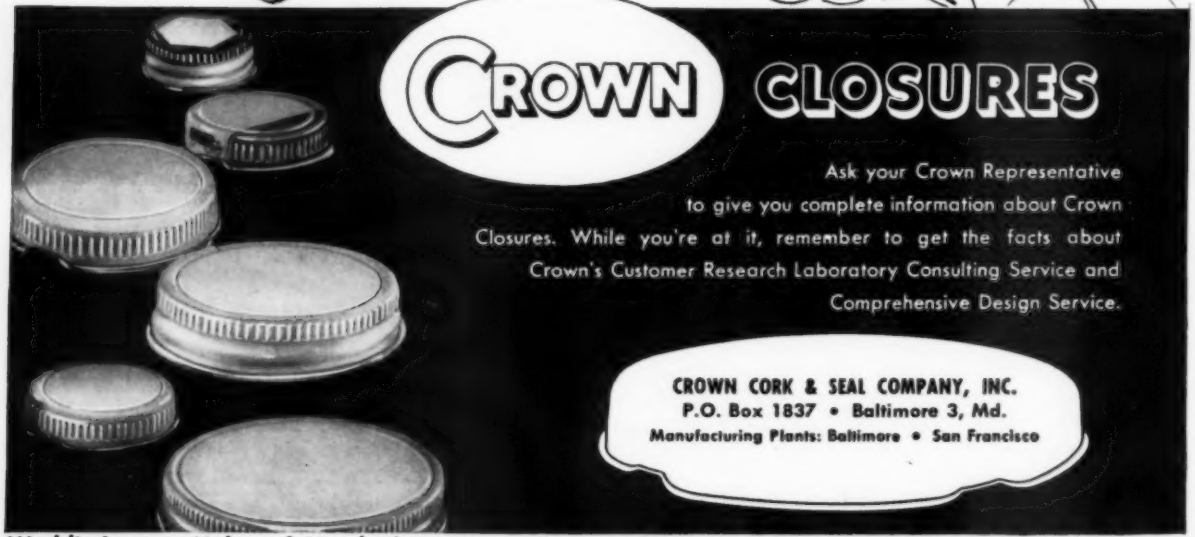
THE PRODUCTION MANAGER is pleased with the way Crown Closures perform on the production lines. These caps assure smooth, trouble-free application . . . a very minimum of lost time due to capping trouble . . . more goods at the end of the day.



THE RETAILER likes to see products sealed with Crown Closures on his shelf. He knows that they are well protected while in stock. The special features of Crown Closures, such as the famous Deep Hook Thread on Screw Caps and scientifically selected liners mean sure protection from packing line to consumers table.

THE CONSUMER appreciates the protection of Crown Closures . . . is enthusiastic about the convenience of these caps. They can be removed easily . . . replaced easily . . . provide a protective reseal over and over again.

And You'll like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Ask your Crown Representative to give you complete information about Crown Closures. While you're at it, remember to get the facts about Crown's Customer Research Laboratory Consulting Service and Comprehensive Design Service.
CROWN CORK & SEAL COMPANY, INC.
P.O. Box 1837 • Baltimore 3, Md.
Manufacturing Plants: Baltimore • San Francisco

World's Largest Maker of Metal Closures . . . also manufacturer of Crown Cans and Merit Seal Closures.

Pond Named Sales Mgr.

Frank N. Pond has been appointed sales manager of Dominion Products, Inc., according to an announcement by Clarence K. Simon, president.

A pharmaceutical chemistry graduate of Columbia University, Mr. Pond has been in sales and administration of the drug, cosmetic and flavor industries for 23 years, having served with the Maltine Company, Fritzsche Brothers, and Dodge & Olcott.

FRANK N. POND

Preston Is Blair Exec. V.P.

Ted D. Preston, former Western division sales manager of Organon Co., has been appointed executive vice president of Blair Laboratories, Inc., Short Hills, N. J., according to Dr. Robert A. Peterman, executive director of Blair.

GILBERT J. STRAUB

Purdue Frederick Vice Pres.

Gilbert J. Straub has been appointed vice president of the Purdue Frederick Company, in charge of the product development division, according to Benjamin Schneider, president.

For the past ten years, Mr. Straub held a similar position with Harrower Laboratory, Inc., Jersey City, which was integrated with Warner-Chilcott laboratories in the recent Warner-Lambert merger.

Cutter-Quimica Argentina

Cutter Laboratories has announced authorization by the Argentine government for the formation of Cutter-Quimica Argentina, a corporation to be jointly owned by Cutter and Serum-Quimica Argentina, S.R.L. of Buenos Aires.

Cutter's first investment in the manufacture of its products outside the U. S., the new company initially will produce only intravenous solutions and disposable infusion equipment. Plans call for other Cutter medical products to be manufactured in the future.

Cutter-Quimica Argentina will be headed by Edme R. Ottati, director of Serum-Quimica Argentina, with technical assistance from Cutter.

Dr. John Paul Snyder

Dr. John Paul Snyder, at one time chief chemist of the Norwich Pharmacal Co. and later a consultant with offices in Washington, D. C., died March 20 at the age of 69.

Colonel Evan Ewan Kimble

Colonel Evan Ewan Kimble, 88, founder of the Kimble Glass Company, now a subsidiary of the Owens-Illinois Glass Company, Toledo, died March 15 at his home in Ventnor City, N. J.

Colonel Kimble received the Scientific Apparatus Makers Association Award in 1951—the second time the award had been given by the association—for his contribution to the American scientific instrument industry and his outstanding work in the chemical glassware field.

When in 1931, before the banking crisis, a Vineland, N. J. bank failed, Colonel Kimble underwrote all school children's savings accounts, believing that these children might lose faith in their community and country if their savings were lost.

Born in 1869, the son of a Tuckahoe, N. J., sea captain, Colonel Kimble went to work at the age of 12 in a Millville, N. J., glass plant. In the early '90s he moved westward, working at plants in Pennsylvania, Ohio and Indiana, and in 1901, with three employees and $3,000, most of it borrowed, he established his own shop in Chicago.

He is survived by his wife, the former Carrie Webb Dougherty, with whom he celebrated their 63rd wedding anniversary December 15; a son, Herman K. Kimble, a director of the Owens-Illinois Glass Company, and successor to his father as president of the Kimble Glass Company from 1933 to 1946; a granddaughter, Mrs. Dale Kimble Ausbrook; and a grandson, Evan Ewan Kimble II.

Carl F. G. Meyer

Carl F. G. Meyer, chairman of the board of Meyer Brothers Drug Co. and former president of the National Wholesale Druggists' Association, died March 5.

From 1916 to 1952 he was president of Meyer Brothers, becoming chairman of the board when his son, C.F.G. Meyer III succeeded him as president. His brother, Adolph C. Meyer, is first vice president of the company.

Chester C. Robinson

Chester C. Robinson, sales manager of the vitamin division of Hoffmann-La Roche Inc., died Sunday, March 25, following a cerebral hemorrhage which occurred while he slept at home earlier in the day.

With Hoffmann-La Roche since 1941, he began his career with the company as a pharmaceutical sales representative in the Chicago area. A year later he was transferred to the bulk vitamin division, serving the same area as sales representative. Given special duties in 1950, the Nutley, N. J., plant became his headquarters. Shortly thereafter he was appointed sales manager of the vitamin division. Prior to his association with Hoffmann-La Roche, he had been president of the Ucoline Products Company.

Born in Indiana Harbor, Ind. in 1904, he attended Howe Military School, Choate School and Yale University.

He is survived by his wife, Mrs. Madeline Robinson; his son, Carter; and his mother, Mrs. Belle Robinson.

Carroll Dunham Smith Sr.

Carroll Dunham Smith Sr., 83, president of the Carroll Dunham Smith Pharmacal Company, New Brunswick, N. J., died March 2 after a brief illness.

Son of Dr. Henry M. Smith and Mary Moorhouse, he represented the third generation of his family in the pharmaceutical industry, continuing an enterprise begun by his grandfather in 1844 as the Smith Company.

Mr. Smith is survived by his widow, Mrs. Carroll Dunham Smith Sr.; a daughter, Mrs. John K. deVries; and two sons, Carroll D. Jr. and deVeaux O. Both sons are associated with the firm.

In deodorizers WATER'S FINE!

Make Your Profit Line with

ORBIS

"AQUASPRAY"
PERFUME OILS

LIKE THIS:
(no alcohol needed)
3 ozs. ORBIS "Aquaspray" Perfume Oils
3 ozs. Formaldehyde Solution U.S.P.
Enough water to make one gallon

COST PER GALLON—ABOUT 38¢

ORBIS shows you economies that make quality products pay. Take ORBIS "Aquaspray." Use it in popular aerosols . . . in all your deodorizers. "Aquaspray," mixed as above, makes a permanent milky-emulsion, air-purifying spray, without costly alcohol. Gives a fresh, clean scent for less than 38 cents a gallon.

ORBIS has all the essentials

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OTHER ORBIS PRODUCTS—Essential Oils . . . Perfume Bases . . . Fruit Flavors . . . Aromatic Chemicals . . . Cosmetic Raw Materials . . . Water Soluble Gums . . . Oleo Resins

Management Forum

by Francis Chilson
INDUSTRIAL CONSULTANT

Diagnosis Inc.

Now that we have discovered the meaning of that wonderful word "automation" after working for a century to make all sorts of things automatic I have decided to apply automation to diagnosis.

It is a well-known fact that most doctors can do almost everything in medical practice but diagnose accurately, in spite of all the gadgets with which they clutter up their offices. Hence, I have decided to apply automation to the practice of medicine to eliminate doctor's mistakes. Parenthetically it must be admitted that the pharmaceutical industry has had much to do with the diagnostic ineptitude of the modern physician. Because of the drugs developed by our industry, a whole galaxy of diseases have virtually disappeared—from small pox and diphtheria to pneumonia. Consequently most of the younger doctors have never actually seen or smelled any cases of the once common diseases; they learned about them from books, therefore, it is no wonder they so often confused a case of mumps with one of fallen arches.

You and I have had too many experiences with diagnoses that were more than wrong. I say "more than wrong" because it often aggravates the disease you have while being treated for something else. Like being operated on for gall bladder when you have a slipped disc.

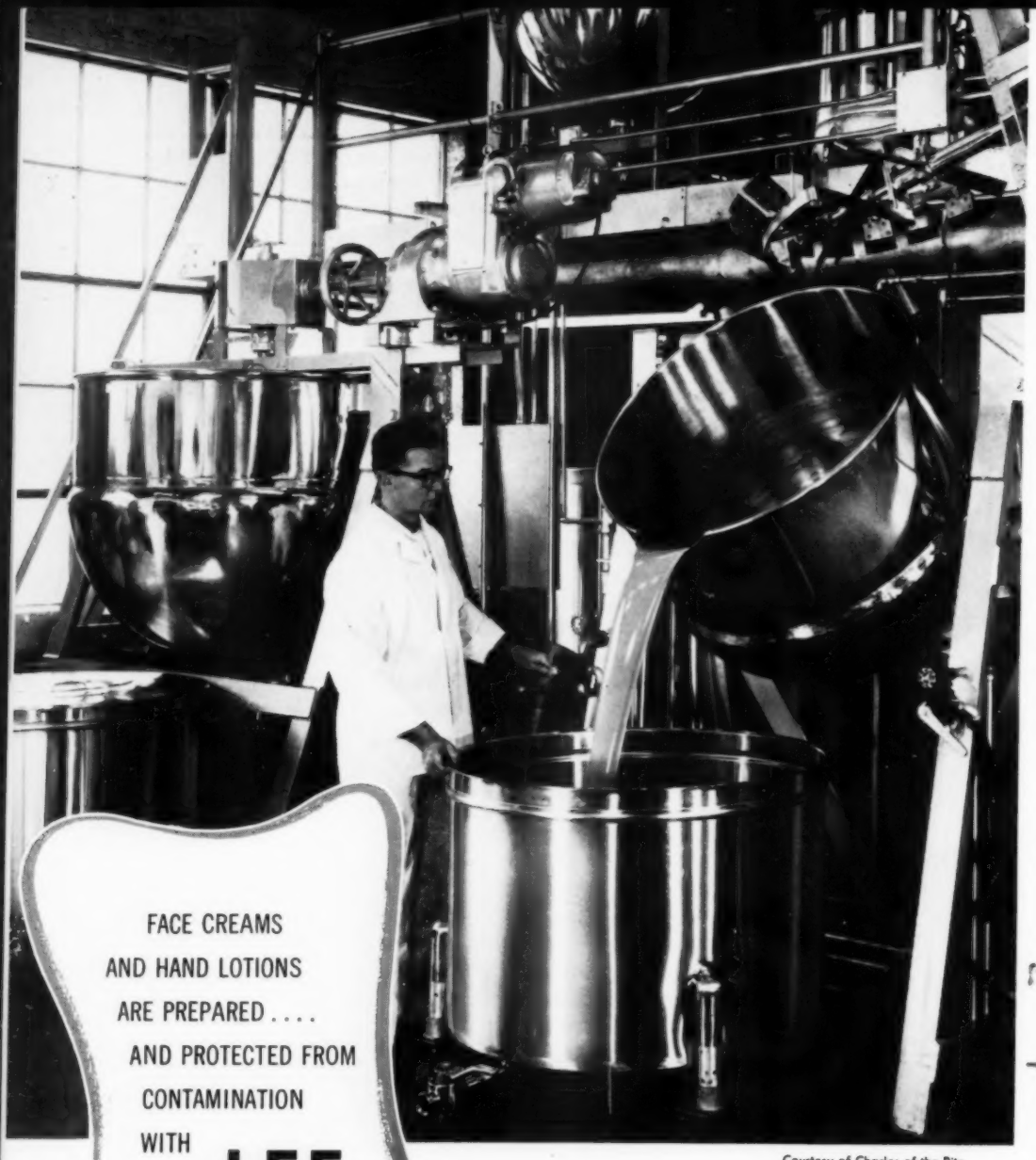
One phase of the history of medicine is the history of bad guesses. But, I am pleased to announce, that all these blunders are of the past. I have invented an electronic diagnostic machine, and have formed a corporation, Diagnosis Inc., to build and distribute the machines. They will be located in all railway and bus terminals, saloons, subway stations, dance halls, baseball parks and wherever busy people foregather or pass by in adequate numbers. You can't buy any stock in my corporation; it's all reserved for doctors (that is all but my fifty-one per cent). (The English concession has been taken up by "Sir John" Walmsley to speed up the practice of socialized medicine in England. It won't be for Royalty only but it will be on a royalty basis.) I must reserve the stock for doctors because I don't want the AMA to sue the machines for illegal practice of medicine. I don't quite know how the AMA would go about suing a machine but they'd probably find a way.

My machine looks like an overgrown slot machine with a pull lever on one side in the conventional manner. This is to make it look as much as possible like a one armed bandit instead of a two armed bandit. Nothing like a professional look. The entire face of the machine is furnished with rows of buttons like an adding machine. Each button denotes a specific symptom and next to the button there is a coin slot. (Fifty cents per symptom.)

On the left side of the machine is a device for making change. You can feed bills into this device between a pair of rollers. As the bill is fed between the rollers, it is scanned by a photoelectric eye which determines its denomination. Just above this device there is a jet, connected with a pressurized slimy water tank, so that if you should attempt to feed a bit of blank paper or a phony bill between the rollers, the photoelectric cell, through a series of relays and a solenoid valve, will open the jet and the machine will spit in your eye. At the same time it will blow a police whistle, ring a bell, sound a horn, flash a red light and holler, "Thief!"

Now suppose you're feeling rotten after having made several futile visits to your doctor or doctors. You are losing weight; you feel irritable, you perspire at night, you cough, especially in the mornings and your sputum frequently is streaked with blood; your pulse is rapid; you suffer shortness of breath; you feel painfully tired all the time; you have chest pains at frequent intervals. That's nine symptoms. Four and a half bucks.

All you have to do is get a supply of half dollars and insert them in the appropriate slots. Then you pull the lever. Presto! out comes a numbered ticket show-



Courtesy of Charles of the Ritz

FACE CREAMS
AND HAND LOTIONS
ARE PREPARED....
AND PROTECTED FROM
CONTAMINATION
WITH

LEE *STAINLESS STEEL* KETTLES

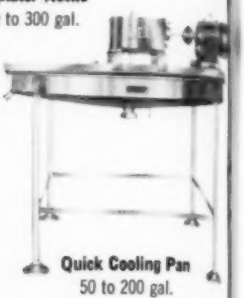
Assuring high quality control in the production of delicate creams and lotions, these Lee steam-jacketed stainless steel kettles are corrosion-resistant and easy to clean and keep clean.

Complete product mixing is obtained through the use of Lee double-motion center line scraper agitators, whose large stainless steel scraper blades continually move the contents from the heated walls toward the center, keeping an even temperature throughout.

Lee hydraulic operated cylinders—using your present water lines—give perfect control and safety not only in tilting the kettles for pouring and cleaning, but also in raising and lowering the tilting agitators.

Descriptive bulletins for all of our specially-designed processing equipment available on request.

CW3T
Center-line Scraper Agitator Kettle
80 to 300 gal.



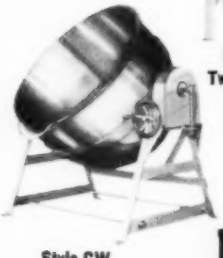
Quick Cooling Pan
50 to 200 gal.

Style A
Two-thirds Jacketed
5 to 500 gal.

Style B
Full Jacketed
10 to 300 gal.

Style C
Two-thirds Jacketed
5 to 100 gal.

Pressure Kettle
Two-thirds Jacketed
40 to 200 gal.



Style CW
Two-thirds Jacketed
80 to 300 gal.

Pulp Tank
500 to 2,000 gal.

Mixing Tank
25 to
500 gal.

Storage Tank — 100 to 5,

LEE

Technical bulletins fully describing these processing units gladly sent on request.

METAL PRODUCTS CO., INC.
418 PINE STREET, PHILIPSBURG, PA.

Designers and Manufacturers of Corrosion-Resistant Processing Equipment for over 25 years.

ing your photograph in color, which was taken when you pulled the lever; also your weight, because you have been standing on a scale without knowing it; your height, pulse rate and blood pressure, measured electronically and printed on the ticket, your disease, which in this case is probably tuberculosis.

You're not finished yet. You take your diagnosis around behind the machine, which is designed in a manner similar to the front with push buttons, each of which is marked with every disease known to man, including a few that aren't. (I had to make the machine flexible to provide for future contingencies when all known diseases have been obliterated and doctors are forced to invent new ones or import them from Mars.)

The back of the machine also has a change maker but in a higher denomination. This one dispenses silver dollars only. There is also a separate device which enables you to bet with the machine for or against your chances of getting better within a specified period of time at any odds you choose. You can't win of course, any more than you can win from a slot machine. You have to insert your diagnosis ticket in order to bet and, as it is numbered, the machine collates it with the punched tape that was made when making the diagnosis. The machine knows the probabilities of recovery, since this information was established actuarilly for each disease and recorded previously on prepunched tapes, which were inserted when the machine was installed. The machine dispenses a bet ticket, dated and stating the bet. If you should win and still live until the stated time ends, you collect by forwarding the ticket to Diagnosis Inc. If you lose within the given period of time your bet is placed in the extra dividend pool of Diagnosis Inc. (Ten per cent of this pool is to be allocated to research.)

Now that you have a supply of silver dollars, having spent a few dollars betting for or against your chances of recovery, (nothing like a bit of fun when you feel sick) you now find youself facing that operating panel of the machine. Across the top there is a row of buttons with local doctors names on them and above the buttons their photographs. You drop a silver dollar into the slot below a doctor's name and pull the handle. If he is in a light appears behind his picture. If he isn't your coin is returned and you try another doctor.

Having made a connection with the doctor—a pure formality of course—you then feed your diagnostic ticket into the machine, after inserting the appropriate number of dollars (each disease has a different price) and you pull the lever again. While you stand there you are being x-rayed and the x-ray is appearing on the doctor's television set along with a precoded interpretation from a prepunched tape. At the same time your body sounds—heart etc. are being broadcast to the doctor from a microphone in the machine. You won't hear these sounds. Professional ethics.

The convenience of my machine to doctors is obvious. It will take them off the daily treadmill. No night calls. No office calls. No longer will they have to look wise at thirty patients a day in order to make a decent living. Since patients will not find it necessary to put in personal appearances, the doctors' waiting rooms will be empty. But the patients' places will be taken by a hungry horde of detail men with whom the doctor will have plenty of time to chat.

The doctor (and stockholder) after looking at your innards and listening to the coded diagnosis and body sounds, consults Merck's Manual and sends a signal to the machine by means of a keyboard on his television set. The machine dispenses a ticket telling you what to do, where to go and whom to see if you should happen to be a surgical case; but if you merely need medicine, the doctor signals a prescription number which then appears on your ticket. If he makes a mistake the machine corrects it and prints the right number on your ticket anyway. The price of the prescription also is printed on the ticket so that all you have to do then is deposit the requisite number of dollars in a separate slot machine, opposite the appropriate number, and out comes your prescription.

Since these machines will be operated under the highest ethical standards, proprietary drugs will not be dispensed—only those made under strictest government supervision by Diagnosis Inc. will be available.

Basic Research

There is no doubt that in the drug and cosmetic industries the majority of managing officials regard research as a necessary but expensive gamble. They are resigned to research as a means of obtaining unique, salable products in—they hope—a reasonably short time. They know many stories of colossal returns received by companies whose researchers hit the jack-pot. (The researchers didn't benefit to the same extent of course.) They hope that by spending annually a few thousand, tax-deductible dollars, they also may hit the jack-pot to the tune of a few millions. However, they regard the investment in research as so risky that they would prefer to buy up other companies, which have established research products, and they also scour the world looking for new, patent-protected products, developed by other companies which can be obtained on a royalty basis. This is a sound, sensible business procedure.

But we must not lose sight of the fact that the purchase of new products cannot go on forever and that new products cannot continue to pour from our laboratories unless the basic research, of which the new products are only applications, is generously supported. Let me repeat: every new, marketable product is only one application of perhaps only one phase of basic research done somewhere, somehow; by somebody, sometime. The very instruments used in research were discovered somewhere by other people.

Lord Kelvin said it in 1883—

"...when you can measure what you are speaking about, and express it in numbers, you know something about it..."

moisture

... is a troublemaker or a benefit, dependent upon your interest and industry. You need to get rid of moisture to keep a process percolating, or add it to promote another. But in most cases, you need to know *when* moisture is present and *how much*.

Moisture in air and gases causes definite phenomena, which suggest methods of measuring amounts of moisture present. These physical facts, and their relationship, have been the subject of extensive research by Elmer R. Queer and E. R. McLaughlin of State College, Pa., consultants to Pittsburgh Lectrodryer Company.

Their findings and recommendations are reported in the new book, The Measurement of Water Vapor in Air and Other Gases—one of a series. You may have a copy.

Lectrodryers* offer a dependable, economical means of removing unwanted moisture from air, gases and organic liquids. Proved in thousands of plants all over the world, they range in size from tiny laboratory models to giant wind tunnel driers. They work at atmospheric pressure up to 6,000 psi. Lectrodryer engineers can call on many years of DRYing experience to help you solve moisture problems. Pittsburgh Lectrodryer Company, 309 32nd Street, Pittsburgh 30, Pennsylvania (a McGraw Electric Company Division).

In England: Birlec, Limited, Tyburn Road, Erdington, Birmingham.
In France: Stein et Roubaix, 24 Rue Erlanger, Paris XVI.
In Belgium: S. A. Belge Stein et Roubaix, 320 Rue du Moulin, Bressoux-Liege.

LECTRODRYERS DRY
WITH ACTIVATED ALUMINAS

LECTRODRYER

* REGISTERED TRADEMARK U.S. PAT. OFF.

The mathematical, physical, chemical and physiological laws that were applied in bringing the new product to fruition were discovered by other researchers in other times and other places. The very line of approach which eventuated in a new commercial product may have been suggested to your scientists by the published results of some obscure researcher, working patiently on the composition of protoplasm in frog's eggs or cell proliferation in sea anemonies. It may seem a hell of a far cry from frog's eggs to face cream or aphrodisiacs (as the case may be) to the man who must put up the dough for the research program, but it also would have seemed in 1928 a far cry from *penicillium notatum* to a specific for pneumonia and gonnorhea. The chances are that if any researcher in 1928 had requested funds to investigate bread mold in the hope that in its exudate might be found a powerful substance, which would virtually obliterate a considerable number of common dissases, he not only wouldn't have got the the money, but the chances are he'd have been fired as being quite mad.

I am quite sure that managers of the large organizations, who have had years of experience with research, understand fully that it is just as important to replenish the basic fund of knowledge as it is to draw upon that knowledge for the creation of additional new products. But I am equally sure that the small and medium sized manufacturers still look upon research from the applied point of view. To hell with everything that went before! Let the universities and the research clinics and the foundations do the basic research, they say. We can't afford to gamble on what may happen in the next ten years. We want results next year. Such an attitude is all very well, but the foundations and other large research organizations must be supported by small firms as well as large ones, and, such an attitude moreover ignores the fact that in the history of research many of the basic discoveries and many of our great products were not discovered by research teams working in large, elaborate air conditioned laboratories, but by individuals working in small, poorly equipped and often poorly supported laboratories.

There isn't a large firm in the drug industry—and I except none—which doesn't thank God for the often meager fellowships it doled out to obscure workers, plodding away in some, even more obscure, pasture-lot colleges. There isn't one of these firms which doesn't thank God for the happenstance that caused some unknown doctor or scientist to suggest an idea to its research division. The basic ideas for the more famous of our products did not always originate in the most famous of our laboratories. This is not said in derogation of those laboratories. It is one of the basic purposes of the research laboratory to attract ideas from outside sources.

These facts are mentioned to emphasize to the small operator, that the basic research gamble is not as great as it seems, that he, too, has a stake in basic research, which cannot be met by merely contributing a few dollars to the Cancer Fund or to some large research institution. These organizations must be supported, too, but the smaller manufacturer should not feel that a small, persistent, (mark the word!) annual investment in pure research under his own auspices must lead inevitably to failure. Even if years of endeavor lead only to the publication of one important paper, it would be a contribution to the backlog of pure research, which, Paul Weiss of the National Research Council, once referred to as the "scientific capital" upon which all who make commercial products must draw. Obviously we cannot forever draw capital out of the bank without putting some in from time to time.

Frankly I used to think that the small manufacturer wasted his time and his money every time he tried a research venture on his own hook. I saw pots of money go down the drain in badly conceived and duplicated research ventures, not only among small companies, but large ones as well. But in the last few years I also have seen research ventures, supported by small companies that not only made important contributions to pure research, but also resulted in the creation of very profitable products.

Research activity in the drug and cosmetic industries is still new and still largely disorganized but it is rapidly becoming organized. After all, the amount of any kind of research done in the cosmetic or pharmaceutical industry prior to 1925 could be written up in a very small book. The pastures are still green and new to us.

I have long felt however that the smaller manufacturers would do well to pool their research funds and activities. Through the trade associations, they have learned to cooperate on legal, control, administrative, sales, tax and production matters affecting all manufacturers, small and large and there is no apparent reason why cooperative research activities would not pay equal or even greater dividends. It is certainly nothing new any more for several companies to put identical products on the market under different trade marks. Secrecy is difficult to maintain in any field of endeavor. Cooperation always pays dividends. It certainly does on control procedures through the contact committees. Why not similar research committees? Other industries have done it successfully.

Bankers on Management

The January issue of Forbes Magazine cites 10 pharmaceutical companies for outstanding management. The yardsticks used are typical of banker's conceptions: Earnings, Growth, Payout & Plowback, Profits vs Plowback. The financial data of all the companies is tabulated in typical banker's fashion. If these yardsticks represent all there is to good management, I am an ignoramus on the subject. I was associated at one time or another with several of the

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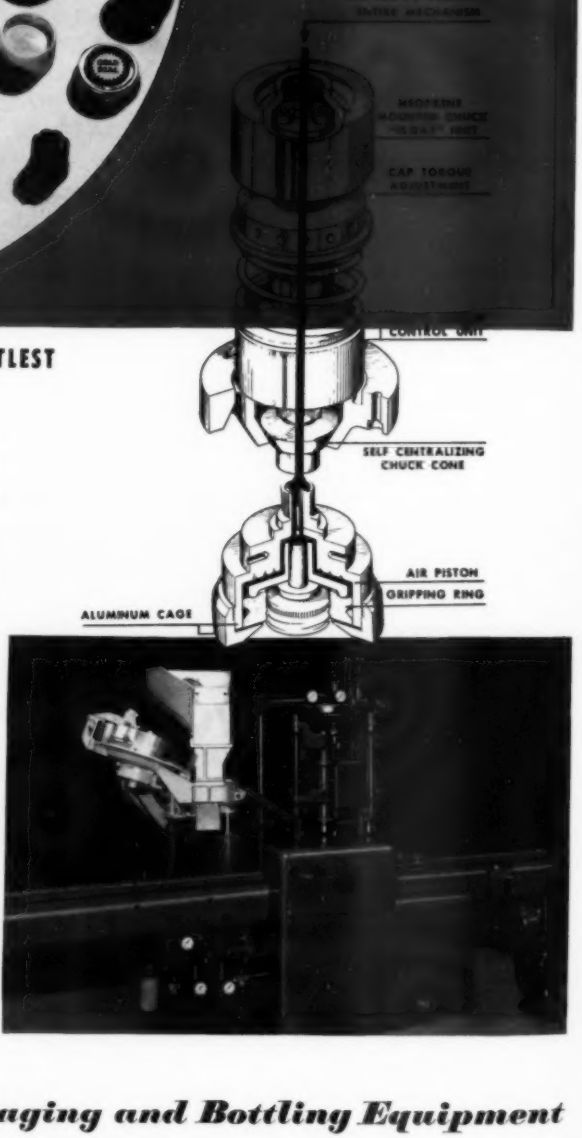

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listed companies and if some of these were or are well managed, I am Chin Lee China Boy. Some of the Big Bens of the listed companies have had the most extraordinary luck in their wildest gambles; but then bankers do not know how to evaluate luck. I wonder if they really know how to evaluate anything?

Bankers Be Banned!

Hear ye! Hear ye! All ye controllers, bookkeepers, budgeteers, auditors, accountants, pennypinchers, scriveners and pencil pushers of various orders and degrees!

Witnesseth:

That I, Francis Chilson, journeyman engineer, professional engineer, management and production councillor do hereby renounce (for the moment) all castigations and diatribes aimed at your individual and several professions and I hereby resolve that from this moment henceforth (unless I should suffer a relapse) I shall confine my diatribes to your masters and my enemies, the stupid bankers.

Item: I belong to a club in New York. A good club. Most members A 1. However a large number of members are a species of vermin known as bank vice presidents. They're thicker than fiddlers in hell and mostly they are members on the cuff because their banks, in the hope of picking up extra business, pay their dues and pick up their tabs.

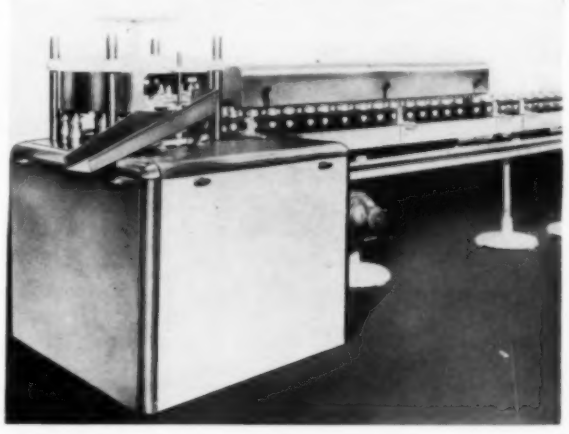
Came one night: I was in the bar, and, in the adjacent pool room, a client of mine with a couple of pals, (he's a bit loud when he is slightly tight), started to play pool on a table next to a pipsqueak V.P. of one of the important New York banks. This jerk took a dim view of my friend's boisterousness. Neither member knew the other. So realizing that he'd been a bit loud, my friend came over and offered his hand in apology. But this little bankbastard refused to accept the proffered apology. He was going to have my friend cashiered. Next morning my client called me and wanted to know who it was who had taken such violent umbrage to him. So I told him. He said, "That silly bastard! My outfit carries an average deposit in his bank of one and a half million bucks! So, he's going to have me thrown out! Well, I'll fix his wagon!" And he did.

Item: I once set me up a little trust account in case I break my neck or have my head blown off by some vindictive controller or bank vice president. (I like presidents and I like vice but I am not partial to the combination.) Anyway you'd have thought I was really an important customer. Everything would be right from then on! It is needless to say that thereafter the bank forgot all about me and my piddling little account. The trust department of the bank bought and it sold; it made money and it lost money. Mostly lost. It made a hell of a lot of clerical mistakes, such as not crediting my account with all the dividends that were collected. So all of a sudden, thinks I, "If I am dead and in a hole six feet in the ground, who's to know that I am entitled to a dividend on my P.D. stock the third Monday after every Tuesday?" So I closed the door with a bang on that bank.

I was all fed up on banks and trust companies. But time heals all. So after a couple of years I tossed my piddling portfolio at a couple of crew-cuts from the Ivy League, who happened to be gossoons for one of the biggest and most reputable trust companies in New York. I knew I wouldn't make much money in dividends by setting up this trust, but I was after GROWTH. That's the stuff! To hell with dividends! After a few years I found that the bankers could lose money as easily as I, and that "Growth" could be a big thing, like a manure heap at the bottom of the ski run, or it could be a nest egg which you wouldn't have had if you hadn't taken the remains of your dough away from the bankers when you did. So I did. I took my skeletal account away from this great financial and statistical organization, which looks after widows and orphans, and which, in a period of two years earned for me a net increment—interest, dividends and capital gains combined of 0.37 per cent! So I say, to hell with bankers! Bad cess to them! I can lose money as well as they do. I don't mind losing my own dough but I hate like hell to hire "experts" to lose it for me.

Fills and Seals Squeeze Bottles

Horix Manufacturing Company, Pittsburgh 4, is offering a machine for automatically filling and heat sealing the new upside-down squeeze plastic bottles.



The sealed filled bottles are automatically ejected onto a conveyor for packaging. Aluminum holders support the inverted plastic bottles and handle them as easily as conventiona containers. The holders incorporate an adjustment feature (inserts) to permit use of one holder for several different sizes of bottles. The entire sealing unit consists of a straight electric heating element discharging to a rotary patter and ejection unit. The length of the heating element will vary according to size of container and operating speed. The machine operates at speeds up to 180 per minute.

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BRIGHTWOOD BOX MACHINES Several models glue and form a broad variety of box styles in a wide range of sizes. Models available for standard single glued end and turned over end boxes. Change-overs are quick and economical.

CANDY AND COUGH DROP CARTONING MACHINES Many filling methods available—by count or by volume—depending on product. Fill an entire range of candy items without use of extra equipment, provided the same size carton is used.

AUTOMATIC TABLET BOTTLING MACHINES Automatic and semi-automatic models accurately count and fill bottles and other rigid containers Machines can be equipped to handle a wide range of tablets, pills or capsules in any desired counts—and there's no tablet breakage.

WEIGHING AND FILLING MACHINES Automatic and semi-automatic models for weighing, volumetric filling or packing. For dry products, free flowing and non-free flowing materials such as coffee, rice, crackers, hard candy, chemicals, cocoa, talcum, food powders, etc.

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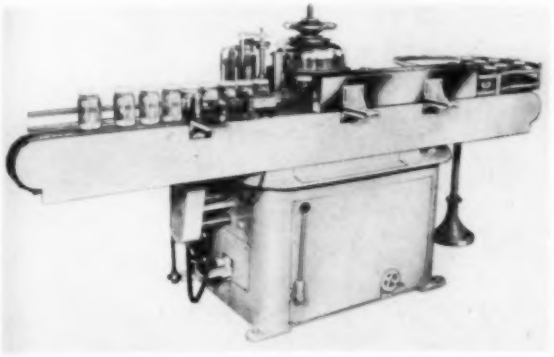
Automatic Labeler

A new 165-per-minute automatic labeler for round bottles, the Pony 165, has been developed by New Jersey Machine Corporation, Hoboken, N. J. The new model features suction labeling (exclusive), non-



stop rotary operation, a circulating glue supply, micro-glue control, shockless bottle feeding, a rotary discharge table, and complete changeover (bottle and label) in 25 minutes. The machine takes any round bottle ½″ to 3½″ in diamater. Maximum label size is 5½″ wide by 5″ high; minimum 1⅛″ wide by ½″ high.

Aphrodisiac

Lecherous Lucullus of old Rome had his own formula for breaking down feminine sales resistance. Here's the recipe. Let me know how you make out:

"Take elcampane, the seeds of flowers (apparently any kind) vervain and the berries of mistletoe. Beat them, after being well dried in an oven, into a powder and give it to the party you design upon in a glass of wine and it will have wonderful effects to your advantage."

Tricky, old devil, what?

Bald When Only

What bald men think about, and what they think about themselves has just been uncovered in a new motivation analysis.

About six per cent of the bald or balding men believe that a receding hairline indicates greater intelligence. Unanimously, all agree that the whispered relationship between baldness and virility is a myth.

About 32 per cent believe that their receding hairline makes them attractive to women. The rest admit they are just average or homely.

One half of the short hair liners wear pink shirts and nearly a third go in for Bermuda shorts.

The age 35 is a critical one. After 35 men accept baldness with resignation.

Washer, Filler, and Capper

Pharmaceutical & Chemical Industry Supply Corp., 16 Hudson Street, New York, is offering a new automatic machine for washing, filling and capping both wide and narrow mouth bottles or jars. Depending on the size of bottle, the machine can be supplied with 10 or 20 filling stations. It will handle up to 200 bottles per minute depending on the size and type of bottle.

New Pressure Filler

A new pressure filler has been developed specifically for packing sudsing or viscous or corros ve cleaning or polishing fluids in cans or squeeze bottles. Low fills and dripping are positively eliminated by glancing at the overflow tubes before raising the head. This filler fills without vacuum thus eliminating collapsing of plastic squeeze bottles or rectangular cans, evaporation of expensive volatiles or perfumes, the need for expensive suds-collecting and -breaking equipment and special ventilation. The machine attains speeds up to 84 twelve-ounce cans per minute and can be

operated by air pressure in tanks, by pumps, or by gravity alone. With gravity alone no power is required which means no electricity or explosion-proof wiring, no water or sewer piping. The filler is available from Laub Engineering Company, 3059 W. Valley Boulevard, Alhambra, Calif.

Contra-Cyclical

You may not have heard it but the advertising boys on Madison Avenue have discovered a new term. This is "Contra-Cyclical Advertising" which means increasing your advertising whenever there is a drop in sales.

It looks to us as if Madison Avenue is getting ready for any possible future development and that they have decided to be well ahead of anything that may happen in building up a business acceptance for the goods which they themselves sell.

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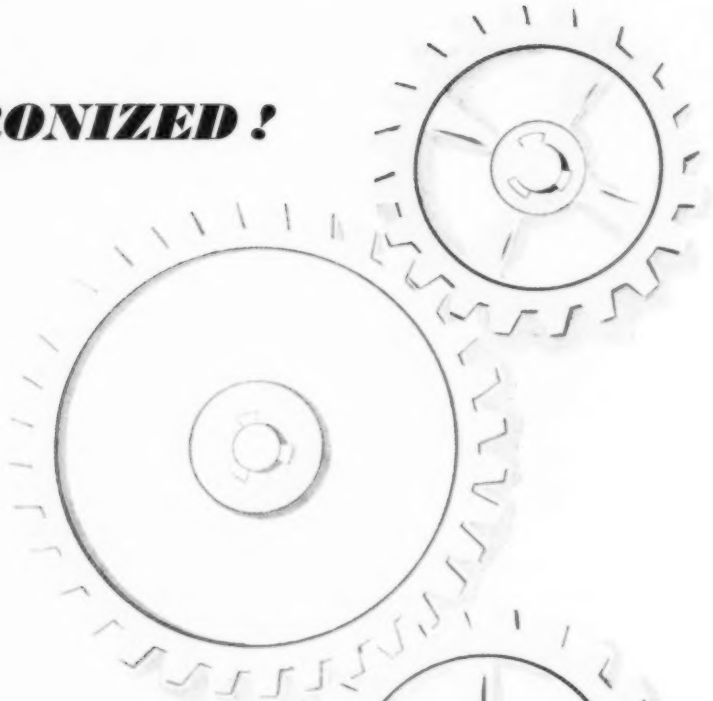

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TYROTHRICIN, U.S.P.

Penick Brand, is a highly purified, stable product. Tyrothricin *was the first commercially available antibiotic.* The Penick Brand is adaptable to broad topical and oral usage.

Though geared for individual, specific uses, these three antibiotics mesh cleanly for a broader, more effective, antibacterial activity. Working together, the practical application of these antibiotics is now extending into cosmetic and allied fields in the form of deodorants, lotions, and dentifrices.

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* *Literature available on request!*

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Advancing Therapy

Cough Treatment

The experimental study of substances for their power to relieve cough is not easy, and hitherto only few attempts have been made. Recently A. F. Green and N. B. Ward (*Brit. J. Pharmacol.* 10:418, 1955) have published the results of observations which they have made in cats, dogs, and guinea-pigs. Coughing was elicited by three methods.

The analgesic substances which were tested for power to suppress cough were given intravenously, and the proportion of animals in which a given amount suppressed the cough reflex was determined. Observations illustrate the variation in the response of different animals, for some cats required no less than thirty times as much morphine as others to suppress coughing. They suggest that a similar variation is likely to be found in man.

The comparison of various substances by this method yielded interesting differences. The surprising result was obtained that methadone was eight times more powerful than morphine in suppressing cough; on the other hand, codeine was ten times weaker. Pethidine was four time more active than codeine. Earlier figures have given higher values for codeine, and there has been very little reference to the use of pethidine at all. High potency was also observed for piperidylamidone (four times as active as morphine) and for thiambutene (twice as active as morphine) but pholcodine was only one-fifth as active.

A satisfactory feature of this investigation was that similar results for the different analgesic substances were obtained whether the cough was produced electrically, mechanically, or chemically. It was also satisfactory that, so far as codeine was concerned, there were no great variations in the sensitivity of the three species of animals which were used. One analgesic is more useful for one patient than another, irrespective of its general relative potency. This seems to be due in part to a variation in the patient's sensitivity to analgesics, and in part to a variation in susceptibility to side-effects. The same is likely to be true when considering the cure of cough.

Soy Sterols

Investigations in recent years have led to the use of dihydrocholesterol and more especially soy sterols (sitosterol) to reduce high blood cholesterol levels. These high levels are presumed to be related to the genesis of atherosclerosis. Actually, the positive evidence that ingestion of soy sterols will reduce high blood cholesterol levels is by no means conclusive. Most recently, G. L. Curran and R. L. Costello of the University of Kansas School of Medicine (*Proc. Soc. Exptl. Biol. Med.* 91:52, 1956) "demonstrate the fallacy inherent in attempts to produce a negative cholesterol balance by inhibition of cholesterol absorption from the gut."

The investigation showed that dietary dihydrocholesterol and soybean sterols were absorbed by rabbits, and soy sterols produced atherosclerosis in these animals. Livers of rabbits and rats fed dihydrocholesterol and of rabbits fed soybean sterols had impaired ability to synthesize cholesterol from isotopically labelled acetate. Rats fed three per cent of soy bean sterols in their diet did not absorb significant amounts of the sterols and the soy sterols failed to produce a lowering of total liver sterol levels in rats.

British Salk Vaccine

The vaccines being prepared by Burroughs Wellcome and Glaxo differ slightly in the strain of poliomyelitis virus used. The Type I strain Mahoney used in the preparation of the Salk vaccine is considered to be unsuitable in Britain, and it has been replaced by a modified Brunhilde strain. In the Burroughs Wellcome vaccine both Type 1 and Type 2 strains are now different from those in the Salk vaccine, and the Type 3 strain will be. The Glaxo vaccine's Type 2 and Type 3 strains are as in the American vaccine — namely, M.E.F.I. and Saukett. Both vaccines will contain antibiotic. In the Glaxo process 200 units of penicillin and 200 μg. of streptomycin per ml. are added to the initial fluid; during the subsequent processing the penicillin is largely inactivated, the streptomycin less so. Thus the final product will contain about 50-100 units of penicillin and something under 200 μg. of streptomycin per ml. In the Burroughs Wellcome vaccine the amount of antibiotic is likely to be similar, and work on the possibility of using other antibiotics is in progress. —*Brit. Med. J.* p. 225, 1956.

Promazine

In view of the recognized therapeutic effectiveness of certain phenothiazine derivatives in the management of patients with disturbed mental states, J. F. Fazekas, P. D. Sullivan and J. D. Schultz (*Med. Ann. D. C.* Feb. 1952) evaluated clinically a new member of this drug series. Animal studies have shown that dimethylamino-n-propylphenothiazine (promazine, Sparine) possesses the same desirable pharmacological properties as chlorpromazine and that its toxicity is of the same order or less.

Patients selected for this study were suffering from a var ety of acute mental disturbances, including such alcohol-induced syndromes as de ir um tremens, acu e hallucinosis, acute tremulousness, and inebriation as well as withdrawal symptoms of drug addiction, and agitation due to various psychoses. Promazine was administered intravenously, intramuscularly, or orally in doses ranging from 50 to 400 mgs.

In 15 subjects with delirium tremens, promazine was administered by rapid intravenous injection. Within five to 10 minutes after completion of the injection, five subjects with moderately

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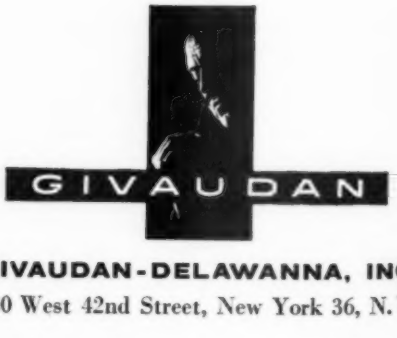

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severe delirium tremens fell asleep; they awakened after five to seven hours exhibiting no evidence of delirium tremens except for residual increased tension.

In six other patients, a second intravenous injection was given after two to three hours, and subsequently satisfactory maintenance was accomplished by intramuscular or oral administration.

Four subjects with severe delirium tremens shows little or no improvement after intravenous administration of promazine. Pentobarbital sodium resulted in almost immediate sleep which lasted from five to eight hours. On awaking, two of these subjects appeared to be asymptomatic while the other two required a second intravenous dose of promazine.

In 32 subjects with the less severe manifestations of alcoholism or withdrawal, intramuscular or oral administration of promazine was usually effective in inducing sleep within 30 to 45 minutes. Oral or intramuscular maintenance therapy for three to five days was attended by complete recovery.

Six patients admitted because of heroin addiction were given promazine orally. Only one of these subjects required supplementary administration of methadon for control of withdrawal symptoms.

Six psychotic subjects exhibiting acute excitement were given promazine intravenously on admission and maintained on oral or intramuscular therapy for as long as two weeks. Initially there was immediate sleep from which the patients could be readily aroused and which in two instances lasted for 24 hours. On awakening, all patients were quiet and tractable and remained so during the period of therapy until transfer to another institution. The clinical effectiveness of this drug and the low degree of acute toxicity appear to warrant further investigation.

Barbiturate Antagonist

Megimide (β,β - methylethylglutarimide) and Daptazole (2-4-diamino-5-phenylthiazole) were administered slowly by intravenous infusion to 56 patients by F. H. Shaw (*Med. J. Austral.* 2:889, 1955) with acute barbiturate intoxication. The patients were brought from a comatose to a less than stuporous condition in a shorter time than eight hours, while with conservative treatment the average duration of coma is 52 hours. Animal experiments show that Megimide produces a reversal of the barbiturate-induced changes in the electroencephalogram of the dog and cat. Common analeptics produced no demonstrable changes in the electroencephalogram of dogs treated with amobarbital. Megimide prevented death in rats that had received twice the lethal dose of pentobarbital, and the antagonism was reciprocal. Megimide also enabled rabbits to survive a lethal dose of thiopental sodium. Megimide, therefore, is to be classed as a barbiturate antagonist and not as an analeptic. The advantages of treatment of barbiturate intoxication with Megimide are as follows: it removes the necessity for prolonged endotracheal intubation; it minimizes both the immediate risk to life and the remote risk that may follow the onset of complications often associated with prolonged barbiturate coma; it affords relief from the burden of prolonged and strict nursing; and it may serve to distinguish barbiturate poisoning from other types of poisoning or differentiate the coma from that resulting from other causes.

Triethylene Thiophosphoramide

A drug that can control breast cancer somewhat as insulin controls diabetes now appears to be a possibility.

It is triethylene thiophosphoramide, a drug in the same chemical family as nitrogen mustard. It is called thio-TEPA for short.

The power of this drug to cause clinical improvement in advanced breast cancer and to slow its further growth was a surprise finding by Dr. Jeanne C. Bateman, clinical instructor in medicine at the Medical School at George Washington University.

Dr. Bateman emphasized that it definitely was not a breast-cancer cure. Rather it is an agent that acts on the blood chemistry of the body in such a way as to combat cancer cells. If its use is discontinued growth recurs. But Dr. Bateman believes she has proved that it does prolong life in many cases.

Of a total of 122 advanced cancer patients thus far treated, 66 per cent have shown definite lessening of the lesion.

Patients who no longer responded to various types of hormone therapy responded to the new drug.

Oral Trichomonacide

Routine examination of vaginal smears of 818 unselected gynecologic patients by A. A. Plenti et al (*Am. J. Obst. & Gynecol.* 71:116, 1956) showed the presence of Trichomonas vaginalis in 258 patients (31.6 per cent). Among 214 routine cultures in pregnant patients, 43 (20 per cent) were found to be positive for trichomonads, when the same diagnostic technique was used. About 60 per cent of these patients had symptoms attributable to the disease. One course of 24 gelatin capsules of 2-acetylamino-5-nitrothiazole (Tritheon), each containing 150 mg. of the water-soluble, stable, crystalline organic compound, to be taken four times daily, was given to 125 patients in whom the presence of the parasites had been determined. Five days after the completion of the treatment course another culture was taken. A parasitological cure was obtained in 46 (37 per cent) of the 125 patients. Sixty-nine patients (55 per cent) had signs and symptoms of moderate to severe vaginal trichomoniasis before the treatment was instituted; 46 (67 per cent) of these became asymptomatic after treatment. Forty-four (35 per cent) of the patients had undesirable side-reactions. Lowering of the daily dose from 600 to 300 mg. and using enteric-coated tablets for seven to 10 days reduced the incidence of side-effects to about five per cent without affecting the parasitological cure rate. Evidence thus has been presented that T. vaginalis can be eradicated by the systemic action of this potent trichomonacidal agent.

New Pharmaceuticals

Neobon (J. B. Roerig & Co.) is a tonic to improve the appetite and well-being of geriatric patients. Each 5 cc. teaspoonful of the fruit-flavored liquid contains 1 mcg. ethinyl estradiol, 1 mg. methyltestosterone, 25 mg. liver fraction, 2.5 mcg. vitamin B_{12}, 0.17 mg. folic acid, 50 mg. ascorbic acid, 30 mg. ferrous gluconate, 0.1 mg. l-thyroxine, 0.5 mg. d-amphetamine sulfate and 10 per cent alcohol. It is available in bottles containing 16 oz. and also in soft gelatin capsules in bottles of 60.

Cal-O-B (Warren - Teed Products Co.) is a source of prenatal calcium along with iron, vitamin D and pyridoxine. Each tablet contains 500 mg. calcium glycerophosphate, 200 mg. ferrous gluconate, 1000 units calciferol, 1 mg. pyridoxine hydrochloride, 50 mg. ascorbic acid and trace minerals—0.12 mg. manganese, 0.14 mg. iodine, 0.1 mg. fluorine, 0.1 mg. bromine, 0.75 mg. copper, 5 mg. potassium, 1.0 mg. zinc, 0.12 mg. magnesium, 0.2 mg. silicon, 0.1 mg. molybdenum, 0.1 mg. boron, 0.1 mg. cobalt. The product is available in bottles of 100.

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Compounder's Corner

Antiperspirant Stick

The Reheis Company, Inc. of Berkeley Heights, New Jersey showed me an antiperspirant stick based upon one of their chlorhydrols that comes close to being what a segment, at least, of this industry has been seeking. The stick is white and rubs into the skin readily and smoothly and contains sufficient alcohol so that it dries very rapidly when applied. It is a little on the soft side, however, and requires a support type of package; this represents an opportunity for individuals to work on this problem on the basis of the Reheis work and perhaps come up with useful improvements.

The aluminum compound used is the relatively new S-5 which has the interesting property of forming jellies when aqueous solutions are mixed with alcohol; incidentally, this gel itself is a very good cosmetic preparation, quickly rubbing into the skin without trace to give effective astringent action.

An aqueous solution of the S-5 aluminum chlorhydroxide complex is mixed with a warm alcoholic solution of waxlike ingredients and then poured into molds, but the nature of the preparation and its ingredients requires carefully controlled manufacture.

The aqueous S-5 solution is made by adding the solid S-5 slowly to vigorously stirred water; stirring is contined until solution is complete. Based upon the analysis of the original material, the finished solution should contain 13.5 per cent of A_2IO_3, and 20 cc. of this solution when mixed with 15 cc. of SDA 40 alcohol should set to a gel in 10 to 45 minutes. The alcohol solution consists of 50 cc. of SDA 40 in which are dissolved by heat 15 grams of Myverol (Distillation Products Industries), 3 grams of Spermatine No. 50 (Strohmeyer & Arpe), 3 cc. of Deltyl Extra (Givaudan-Delawanna) and 2 grams of cetyl alcohol. This alcohol solution is maintained at 75 to 80° C. until it is homogeneous, avoiding evaporation loss as much as possible and 40 cc. of the S-5 solution added without preheating and with stirring. The solution is heated until it begins to thicken, allowed to cool with agitation to 40° C. when perfume is added and then poured into containers. The finished preparation will contain 6.2 per cent of aluminum oxide, or more, depending upon the alcohol loss.

Electron Sterilization

Escap—electron sterilized capsules—culminates the first investigation by the pharmaceutical industry of the possibility of sterilization by means of ionizing radiations and constitutes the first practical application of cathode ray sterilization to drug products. Escap Neo-Cortef, a sterile ophthalmic ointment in a sterile gelatin applicator capsule within a sterile plastic container, is the first marketed pharmaceutical product produced by this method. The fact that this product retains full label potency and at the same time meets satisfactorily U. S. Pharmacopoeial standards establishes the feasibility of electron sterilization. Moreover, the ability of cathode rays to penetrate substances without appreciably raising their temperature and usually without otherwise altering them makes it adaptable to the sterilization of heat sensitive materials.

Escap is the result of six years of interest in the field of radiation sterilization at Upjohn and, since 1950, of experimentation with a Van de Graaf electron accelerator which was bought and installed in that year at a cost of $100,000, an outlay which represents, of course, only the initial expense involved in pioneering a research development such as this.

Drug preparations studied at Upjohn for their adaptability to electron sterilization have included antibiotics, hormones and steroids, multivitamin formulas, proteins, alkaloids and sulfonamides. The dose which would destroy all bacterial contamination was determined. Under optimal conditions most drugs are stable when submitted to the sterilizing radiation energy; some can sustain doses many times the sterilizing dose without damage. As with foods, however, each drug poses its own problem. In some cases the physical state of the drug must be modified to make it amenable to sterilization. For example, some drugs which cannot be sterilized in solution without substantial loss of potency may, in the dry, lyophilized or frozen state, be entirely stable when subjected to the same radiation. Others may need to be sterilized under vacuum or an inert atmosphere. To illustrate, vitamin B_{12} will decompose if it is irradiated in solution whereas in the dry state it remains stable.

To insure that electron sterilization would not increase product toxicity, acute and chronic toxicity tests were made in animals by comparing the effects of equivalent amounts of irradiated and nonirradiated material from the same lots. Animals were checked for weight change and gross appearance and were then sacrificed and their tissues examined. No essential differences were found in animals receiving any of the materials irradiated with the usual sterilizing doses. It was not until radiation doses were used which were considerably in excess of the sterilizing dose and which may have initiated chemical breakdown that there was any indication of increased toxicity from the irradiated materials. With some drugs such as sodium penicillin G there is a much smaller margin between sterilizing and radiation decomposition doses than with others like potassium penicillin G where they are widely separated.

Because of the limited depth of penetration of cathode rays (which is proportional to the energy potential used) and the fact that all parts of a container must be penetrated to insure sterility of its contents, electron sterilization is more suited to unit dose packages of

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the type used for Escaps than to more bulky products in glass. In its present state of development electron sterilization is only applicable to certain types of products and is still a relatively expensive procedure.

Uvinuls

A bulletin describing Uvinuls, ultraviolet light absorbing compounds, has just been published by Antara Chemicals, a sales division of General Aniline and Film Corporation. These compounds are intended to screen out wave lengths of light up to the visible range, since these rays are responsible for product deterioration due to light. The compounds will protect plastics in which they are incorporated against light deterioration and also will permit transparent plastics to act as sun screens for materials sensitive to ultraviolet light radiation.

Although no toxicity and skin irritation data are given for these substituted benzophenones, they may warrant investigation concerning their usefulness in sunscreening cosmetics where full protection from sunlight may be desirable.

Antiperspirant Stick Patent

U. S. Patent 2,732,327 was issued January 24, 1956 to W. K. Teller and assigned to Pharma-Craft Corporation, the application being dated July 5, 1955. It covers the use of sodium zirconium lactate in alcohol-soap stick deodorant compositions, the first claim being for "A stable antiperspirant stick having a base comprising a sodium stearate-aqueous alcohol gel and having dispersed therein within said base as an active anti-perspirant agent sodium zirconium lactate."

Formulas given as examples are:

Alcohol (95 per cent)	**69.00**	**81.80**
Sodium stearate	**6.90**	**6.90**
Water	**12.80**	**—**
Carbitol	**1.40**	**1.40**
Sodium zirconium lactate (43 per cent solution in water)	**9.20**	**9.20**
Perfume	**0.45**	**0.45**
Hexachlorophene	**0.25**	**0.25**

Shampoo Opacifier

S. Epstein, C. F. Fuchs and M. M. Gladstone, in U. S. Patent 2,733,212, issued January 31, 1956, suggest the use of opacifying agents in shampoos which do not reduce the foaming power. These substances, for use in liquid, paste or cream shampoos, are ester-amides of hydroxyalkyl primary amines with normally solid higher molecular weight fatty acids. Typical of such ester-amides is the stearic acid ester-amide of monoethanolamine, $C_{17}H_{35}CONHC_2H_4OOCC_{17}H_{35}$. These additives may be used to the extent of two to five per cent.

Hair Waving Chemistry

Largely as a result of the valuable studies of J. B. Speakman and his coworkers, we now have a most reasonable general picture of the whole process of permanent waving as applied to human hair according to F. M. Freeman and G. T. Walker (*Manuf. Chem.* 27:10, 1956). Our theoretical ideas concerning permanent waving have emerged only as a result of much brilliant experimental work and imaginative speculation. As the years go by, it seems less and less likely that Speakman's theories will require drastic modification in the light of newly-discovered experimental data.

Speakman's theoretical approach may be briefly described as being centered upon the disulfide bonding system which is known to be an important structural element in keratin, as in other proteins. The disulfide link is pictured as being able to "bridge" adjacent polypeptide chains, thus giving the whole protein structure greater rigidity and cohesion. Speakman considers that the action of steam and of alkaline materials on keratin results in hydrolytic cleavage of the cystine disulfide bonds, with liberation of sulfydryl (—SH) groups. Reduction of these disulfide bonds enables the hair to become pliable enough to assume the shape of the curler. When this stage is reached, an oxidizing agent is applied, in order to set the hair "permanently" in a curled state. The oxidizing agent acts simply by oxidizing the sulfydryl groups back again to disulfide "bridges."

This is, of course, a very much simplified account of what actually takes place during the permanent waving operations; it does appear, however, that the rupture and reformation of the cystine disulfide linkages within the keratin molecule play an extremely important role in the chemical treatment of hair and wool.

Beeswax Emulsions

It is well known that additions of certain hydroxyl-containing compounds to surface-active agents often result in improved emulsifying performance. The acids present in beeswax form soaps with bases and it is possible that the alcohols present in the wax form complexes with the soap to produce emulsifiers which are responsible for the peculiar properties of beeswax.

In order to determine the effect of the beeswax alcohols on emulsions made from this wax the free hydroxyl groups were blocked by acetylation by J. Pickthall (*Manuf. Chem.* 27:56, 1956). Acetylated beeswax lacks many of the admirable emulsifying properties of the untreated wax. A cold cream made from the acetylated wax posesses larger particle size and is relatively unstable when compared to the normal cold cream.

To some extent the performance of this cream can be improved by reintroducing compounds which contain hydroxyl radicals. It would appear that cetyl alcohol is too oil-soluble and the ethylene oxide condensate too water-soluble adequately to replace the alcohols removed by acetylation.

Further work has shown that a careful selection of other hydroxy compounds used in their correct proportions in conjunction with acetylated beeswax will lead to a cream quite as good as the cream made from the untreated beeswax. In fact, it is fair to say that the additions have, in some respects, resulted in creams with improved properties. Cream A, which may be regarded as a "normal" cold cream, can be greatly improved in many ways, (*e.g.*, smaller particle size, better appearance, inhibition of water-loss, stability of the emulsion), by the addition of small amounts of hydroxy-containing materials. The fact that acetylation does not greatly affect the properties of beeswax as a w/o emulsifier is not surprising. The formation of calcium soaps with the beeswax acids results in a reasonably efficient w/o emulsifier and its properties would not be greatly influenced by small additions of alcohols.

Tallow Alcohol

Tallow alcohol in convenient flake form is a new product now being manufactured by American Alcolac Corporation, Baltimore. Trade-named Sipon TX, it is, according to the company, "the lowest cost fatty alcohol on the U. S. market."

Because of its low basic cost and unique properties the alcohol is currently finding application as a detergent intermediate, foam depressant and emollient. It also holds promise as a new "building block" for the manufacture of lubricating oil additives and as a base for the synthesis of polymerization modifiers and emulsifiers.

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Skin Research

Emulsions and Keratin Hydration

The degree of pliability of normal keratin is a sensitive indicator of the amount of water it is able to bind. Two sources of water are available to keratin in its physiological state: that from sweat and the atmosphere and that received from below through a hypothetical barrier. The former source varies seasonally and moisture received from below may be insufficient to maintain pliability under conditions where water is rapidly lost by evaporation. When chapping occurs, treatment consists of the application of an oil film to retard evaporation.

Blank has shown that the pliability of callus decreases after treatment with both water and with various solvents. Callus so treated remained less flexible even at temperatures and humidities where untreated callus remained soft, and even though the treated callus held the same or even an increased amount of water.

Oil-in-water emulsions may be formulated to provide an excellent water-retaining film at lower relative humidities. Their physical characteristics vary greatly with formulation and J. B. Shelmire, Jr. (*J. Invest. Dermatol.* 26: 105, 1956) investigated various types of oil-in-water emulsions with regard to exchange of water vapor.

The investigation was done with small sheets of callus, dried to brittleness and then treated with the emulsion to determine the effect on pliability. A variety of emulsion combinations were tested, the compositions being not too clearly defined; lanolin was conspicuously absent.

It was found that regardless of ingredients, a certain minimum viscosity was necessary to achieve maximum flexibility; this could not be obtained by emulsifying liquid oils alone, but the addition of certain hydrating agents and emulsifiers led to maximum flexibility. Emulsions containing glycerin, as well as other preparations showed little difference in rate of hydration of the callus sheet. Hygroscopic substances do not appear to increase the rate of passage of water into a naturally hygroscopic substance such as keratin. Changes in the oil phase appeared to make little difference as long as an emulsifier was present.

The lipids presumably emulsified in keratin must be primarily in an oil-in-water emulsion or the horny substance would not be able to exchange water as rapidly as it does under extreme conditions. If this is true, both water and solvent substances may remove lipid and emulsifier together, decreasing the total amount of water that the horn is able to bind, hence decreasing relative pliability.

Certain types of oil-in-water emulsions are unique in that they show this water barrier characteristic at low relative humidities, maintaining it for an effective period, while permitting rapid diffusion of water at high humidities. This property is not shown to any extent by water-in-oil emulsions or greases.

Comment: Although data in this paper are sparse, the conclusion reached is that emulsions are superior to oils alone in acting as occlusive films to maintain skin moisture. Repetition of this work, in terms of cosmetic raw materials and well-formulated cosmetic emulsions might well prove profitable with respect to the formulation of superior treatment cosmetics and their promotion.

Skin Physiology Review

R. Kooij, in *Dermatologica* 112:62, 1956, reviews literature on the physiology and pharmacology of the skin and useful portions of his paper are being reproduced here, although much of this material has previously been abstracted for this department.

Lieflander, Tronnier described a new method by which the content of sulfur-containing amino-acids in the skin and their appendages can be accurately determined. With this method they found that the cystine values in the functionally different parts of a healthy skin and more particularly in pathological specimens, showed considerable differences, while the methionine values did not vary.

Hougen demonstrated polycyclic hydrocarbons in human hair wax. From the variety of polycyclic hydrocarbons found, it seemed unlikely that these were all metabolic products. A more plausible explanation according to the author is that the hair acts as an air filter and is, therefore, a good collector of atmospheric soot, which contains polycyclic hydrocarbons. Hougen also isolated twelve aliphatic alcohols of human sebum and identified them.

Kile investigated some mineral constituents of nail clippings from finger nails of both men and women with hard and brittle nails. There was no evidence that brittleness and hardness of nails are related to their calcium or phosphorus content.

Miescher et al. split up fatty acids obtained from human sebum into their separate components. They tested the bactericidal action and found the strongest bactericidal action (on hemolytic streptococci, E. coli and staph. aureus) by the lower and medium fatty acids (up to 10 C-atoms). The highest degree for unsaturated fatty acids was shown by fractions with the lowest C number. Enderlin et al. described a simple method for demonstrating the aspect of the sebaceous layer on the skin surface and estimating colorimetrically the quantity of lipids by paper tests using osmic acid. They found the replenishment time for different methods of cleaning to be practically the same (three to four hours). Kerk, Efferse compared the effect of washing with soap and with a detergent on the four-hour sebaceous secretion in the forehead of 25 elderly subjects. No significant difference was noted. Lapiere showed that local applications of sexual

hormones to the shaved skin of mice had the same influence on the volume of the sebaceous glands and on the frequency of mitosis as internal administration. The acid-free pure olive oil used as solvent interfered with the results; an ointment containing carbowax and propylene glycol did not. The androgenic hormone had a considerably stronger stimulating action on the sebaceous glands in male, and the oestrogens a stronger inhibiting action in female animals. Jarrett demonstrated in six patients with acne vulgaris a significant reduction of the surface sebum following the oral administration of 3 mg. stilbestrol a day. The acne also improved but there was a tendency to relapse when the treatment was stopped. Histochemical methods applied to biopsy specimens taken before and after stilbestrol treatment failed to show any alteration in the nature of the fat in the sebaceous glands, or any significant change in their glycogen content. Brun et al. described a semi-quantitative method with paper tests which makes it possible to evaluate a local sweating effect in man. Twenty-one sweat-stimulating substances introduced into the skin by iontophoresis were studied and classified according to their activity.

Kanof studied the effect of 8-methoxypsoralen applied locally and followed by solar or ultraviolet radiation in eighty-five subjects. The cosmetic results was acceptable in only six. Natural sunlight in combination with the drug was superior to irradiation from various ultraviolet generators. The psoralens can be activated not only by rays of the known "erythemogenic band" (below 3200 A) but also by rays of longer wavelengths (up to 4000 A). Behrman compared the effects of creams containing 7500-15,000 I.U. of estrogen/ounce with those of the same creams without the hormone on the facial skin of women. The jars of cream were inlabeled, one was applied to the right side of the face, the other to the left side. No definite differences could be detected. Ramsy, Jones studied the adsorption of soap on the skin. Cleansing with water alone or with alcohol results in no alteration in the normal lipid layer on the skin. During normal cleansing with soap and water an adsorption of soap is formed on the skin. This soap layer is converted in the course of 25-60 minutes into a layer of free fatty acids which clings tenaciously to the skin and might be detrimental to it. Baer tested the germicidal action on human skin of a soap containing one per cent tetramethylthiuram disulfide. It is concluded that this soap is a highly effective germicidal agent for use on human skin. The allergenic sensitizing capacity seem to be low. Shaw, Crowe tested the effectiveness of several protective ointments. The best results gave those, containing silicones. The most effective protection was provided by a mixture of 30 per cent silicones in petrolatum against a wide range of aqueous solutions. Thurmon et al. studied the sorption of amino-acids and other substances by amberlite ion exchange resins. Ion exchange resins have the sorption capacity to remove amino-acids *in vitro* and the amino-acids present in human perspiration. They were found to be bacteriostatic for staph. aureus and fungistatic for Monilia albicans in direct proportion to the concentration of the resin in the culture media. Ikai showed that the lower fatty acids were absorbed and deodorized by anion exchange resins. Ammonia was absorbed and deodorized with exchange resins and indole by cation or anion exchangers. Odor from the secretions of the axillae was absorbed well by any exchangers, but heretoo, the mixture of cation and anion exchangers were more powerful. Cornbleet, Joseph determined the initial pH of the skin of the dorsal surface of the hand potentiometrically with quinhydrone electrode in normal persons and those with atopic eczema. The latter showed greater fluctuations in the alkali-acid retention curve. Cationic exchange resins were employed to modify the effects of alkali and soap on the skin. Shapiro et al. studied the toxicity of selenium disulfide suspensions by using tissue culture techniques first on chick spleen then on human skin. It was shown that 2.5 per cent selenium disulfide suspension was no more toxic than the vehicle alone.

Effect of Drugs on Serum Sulfhydryl

There is considerable experimental evidence that during keratinization of the skin, the sulfhydryl (—SH) groups of the stratum granulosum are converted to disulfide (S—S) groups in the stratum corneum. Vitamin A has been extensively prescribed for modifying keratinization of the skin. Flesch has shown that Vitamin A "ties up"—SH groups in skin and liver homogenates of rats. Many different compounds of widely varying chemical structure have been introduced into living animals to produce specific biological effects, therapeutic or otherwise. There is reason to believe that certain of these drugs produce their effects by inhibiting or otherwise acting upon the thiol (—SH) systems.

In dermatologic practice, para-aminobenzoic acid, sulfanilamide, gantrism (sulfasoxazole), 8-methoxypsoralen and atabrine are frequently prescribed for systemic administration. The effects of these drugs on the —SH and S—S groups of *in vitro* sera were investigated by R. W. Goldblum, W. N. Piper and C. J. Olsen (*J. Invest. Dermatol.* 25:139, 1956) both with and without ultraviolet irradiation. It was believed that an evaluation of the effects of these drugs would give further insight into the mechanisms by which they control keratinization.

In each case where serum was irradiated without the addition of a drug, there was an increase in the sulfhydryl level (Figure 2). When a drug was added to the non-irradiated serum, the —SH level did not change significantly. The time of incubation (15 to 45 minutes), did not have any effect.

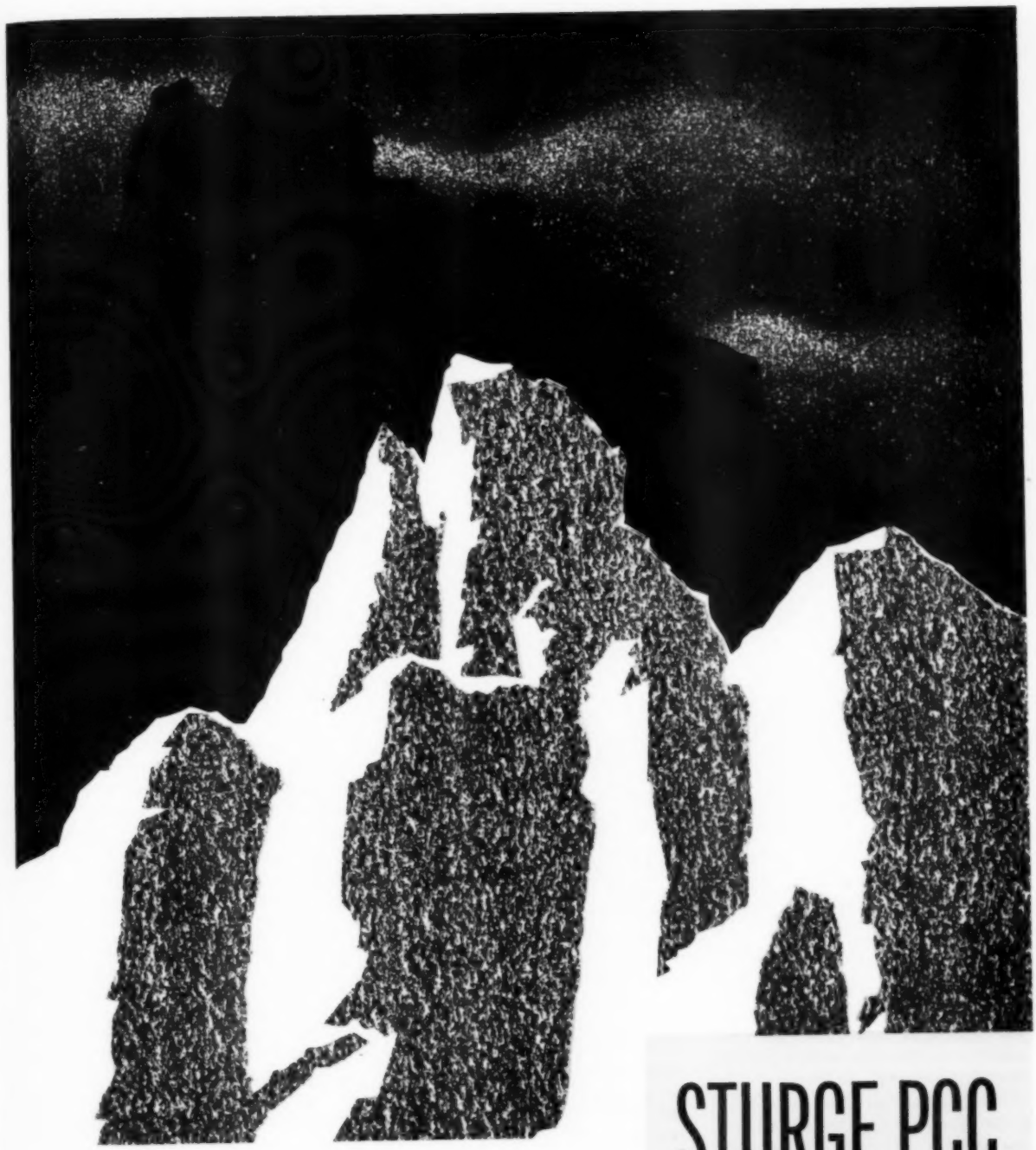
When the serum, containing the atabrine or the 8-methoxypsoralen was irradiated, the —SH level increased, but the increase was not so great as when the serum alone was irradiated. The presence of these drugs somewhat inhibited the rise in —SH groups.

Sulfanilamide, gantrisin, and para-aminobenzoic acid (PABA) exhibited a striking action on the concentration of sulfhydryl groups, when the sera were irradiated. In these three cases, the —SH levels after irradiation were found to be much lower than the levels of normal non-irradiated sera. If the drugs were added after irradiation, they caused no significant change in the irradiated levels. An interesting sidelight of the effect of PABA was its inhibiting action upon the oxidation of serum sulfhydryl groups.

Polycycline for Acne Vulgaris

In a study involving seventy-two acne patients, the Polycycline produced satisfactory clinical response in ninety per cent of the cases of acne according to a report by Dr. G. A. Cronk and associates in the A.M.A. Archives of Dermatology.

The investigators observed that, since acne is not merely a simple bacterial infection but also involves hormonal imbalance within the body, the beneficial results obtained in the tests indicate that the antibiotic exerts more than a germ-killing action.



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Perfumer's Shelf

Essential Oil Uses

The most obvious applications of essential oils in medicine are as flavoring agents to mask unpleasant drugs and also to take advantage of their mild irritant action on the digestive tract with consequent stimulation of the appetite and relief of indigestion. Essential oils also act as expectorants, counteract the griping action of purgatives and exert a rubifacient effect on the intact skin. These oils are quite largely used as counter-irritants in the treatment of inflammatory conditions and for the relief of neuralgia and rheumatic pains.

Some essential oils by virtue of their phenolic content and other constituents are quite powerful antiseptics and as such are used in dental preparations and to check the growth of fermentative micro-organisms in the stomach.

Pharmacists will be familiar with the application of essential oils such as citronella, lavender, lemongrass and geranium as insect repellents. During World War II investigations were made into possible applications in this field of certain Australian oils containing phenol ethers. The leaf oil of *Backhousia myrtifolia* contains about 80 per cent of elemicin. During the course of this work it was discovered that these oils while being non-toxic to flies acted as powerful synergists in pyrethrum sprays.

The development of aerosols or colloidal mists will undoubtedly increase the use of essential oils and other aromatic products in deodorants, insecticides, sun-tan oils, disinfectants and perfumes. The formulation of these products calls for rather specialized knowledge of the nature of the aromatic materials employed and careful selection of the appropriate propellants.

A few essential oils have a blue or greenish tint due to the presence of one or the other of a group of hydrocarbons known as azulenes. These colored compounds do not pre-exist in plants, but are formed during the steam distillation of chamomile flowers, wormwood herb, guaiac wood, etc. Blue azulene has now been produced synthetically in commercial quantities and is stated to exert a beneficial action in inflammatory conditions of the skin and mucous membranes. In cosmetics this compound has been used to protect the skin from pimples and pustules and also in tooth pastes and gargles.

One of the most difficult problems confronting flavor chemists is the provision of flavors for masking unpleasant medicines such as the bitters and saline substances like ammonium or magnesium chloride. Many of the old favorites are still very useful, examples of these are cherry, aniseed and cloves for cough syrups and liquorice for saline drugs provided these latter are not acid in reaction. Bitter drugs are rendered more palatable by the use of blends of oils having a sweet character, such as anise, coriander and fennel either with or without saccharin. Lemon, orange, lime and tangerine oils add brightness to flavor blends, but if deterioration is to be avoided it is preferable to use the terpeneless oils or soluble essences prepared from these oils. Acid medicines are usually improved by the addition of fruit flavors. Fruit and chocolate syrups find favor with children, as do butterscotch and vanilla. Paraldehyde is particularly difficult to mask, but peppermint oil is probably the best flavor to use for this. Cod-liver oil preparations are greatly improved by the addition of citrus oils which latter may be blended with or without the use of vanilla or a trace of almond. For penicillin lozenges one can hardly improve upon oils of lemon, orange or lime, but when these have to be stored for some time it is better to use the powder form of these flavors. Amino acids and powdered liver or extracts of liver lend themselves to the use of spice and savory essential oils such as ginger, cinnamon, parsley and celery. Many essential oils, in common with vanilla, have the property of anesthetizing the taste buds, thus assisting in masking unpleasant flavors.

Tooth pastes are a fertile field for the use of essential oils, not only for their flavor value but also for the feeling of freshness imparted to the breath; here again the bactericidal activity may be a consideration. Among the more commonly used oils for this purpose are peppermint, spearmint, anise, clove, caraway and rose, but the citrus oils may be found useful as blenders.—G. R. A. Short, *Pharm. J.*, p. 75, Feb. 4, 1956.

Taste

The taste, smell, and appearance of a pharmaceutical preparation are matters of no mean importance; a fact recognized by the early medicine makers, who concocted as medicine some of the liqueurs we now prize solely for their flavors. Since to the ill patient these considerations are of particular importance, a prominent factor in the rise of the pharmaceutical industry has been its ability to prepare medicines that have good appearance and flavor.

While the organs of taste and smell are distinct and the impulses from them reach the cortex by totally different pathways, the two senses are closely associated psychophysiologically. They are designated as chemical senses, because chemical rather than physical stimuli act on the receptors. Taste proper is the less discriminating of the two, and the most important aspects of flavor are olfactory rather than strictly gustatory. A person whose sense of smell has been impaired or destroyed can still distinguish certain flavors by varying combinations of the primary tastes—sweet, sour, salt, and bitter. But the spectrum of gustation is short and, because of lack of quantitative discrimination, almost devoid of shading. Olfaction, on the other hand, detects many odors and is also sensitive to small changes in concentrations of them. Because of this it is capable of crudely

ascertaining the direction and distance of the source. In addition to these chemical sensations, touch, temperature, and pain sensations originating in the tongue and buccal cavity contribute to taste impressions the appreciation of texture, temperature, and spiciness.

Probably less is known about the chemical senses than any of the others. Scientific studies of them have been handicapped by lack of instrumental methods for detecting chemical substances in the minute concentrations to which the nose is sensitive. While some attempts have been made to explain how these tiny amounts of chemical materials can give rise to nerve impulses, such as possible interference with enzymatic reactions, there is still insufficient knowledge for the formulation of a reasonably probable working hypothesis.—*Scope* (*The Upjohn Company*) 4: No. 8, 1955.

Neroli and Orange Flower Replacements

Europe's worst and longest cold wave has damaged flower cultures of Southern France and Italy, particularly orange blossoms; latest reports indicate an infinitesimal crop for 1956 and reduced harvests for 1957 and 1958. Replacement of Neroli Bigarade and Fleur d'Oranger Absolute, valuable raw materials in creative perfumery, is a serious problem. As a contribution to the solution of this serious problem, Felton Chemical Company is offering Nerolyol No. 632 and Fleur d'Oranger Alternate No. 7, faithful and full-strength reproductions of the true Neroli oil and Orange Flower Absolute incorporating the newest aromatic bases developed in the Felton research laboratories.

Roure-Dupont, Inc. is also offering specialties to relieve the forthcoming shortage. These include Neroli Petales, Neroli 1956, Neroli 256, Fleur d'Oranger Synthetique and Fleur d'Oranger Synthetique 1908.

Animal Odors

In the synthetic reproduction of musk, research has led to three main chemical groups. Two of these groups are the large ring ketones and the large ring lactones. The third group, the nitro-musks, provides important perfumery synthetics, known as Musk Xylol, Musk Ketone, and Musk Ambrette. None of these could properly be called a perfect musk reproduction, but each have merits.

The odor of musk actually is the most intense odor we know. Minute quantities are sufficient to impart to a large body of air the characteristic odor. Fresh musk has a powerful nauseating odour, just as we do not know with jasmine whether its odor is pleasant or repelling.

In very dilute alcohol solution the odor becomes fragrant and gives other perfumes a curious and highly prized bouquet. Tonkin musk, musk tonquin, constitutes about 80 per cent of the world's supply. The finest musk is called hankiu musk. It is very rare.

As a fixative musk is among the best in the realm of perfumery. Musk is used for the finest soaps and sachets, and in minute quantities in the manufacture of the most expensive perfumes.

Civet is the secretion of a gland both in the male and female civet cat. The gland is located near the sexual organs of those animals. In captivity the fatty yellow substance of which the male produces the larger amount, is removed from a deep pouch about every two weeks.

Civet, another effective fixative, is said to round out or to bouquet a perfume. In a jasmin compound, *e.g.* tincture of civet will take the rough edges off the benzyl acetate. Civet contains some skatole, a highly malodorous material which can be produced synthetically. The main contribution to the odor of civet is the ketone known as zibethone or civetone, a high-boiling substance that has also been duplicated by synthetic means.

Castor or castoreum is a secretion of the beaver. Most castor used in America and Europe originates from the Canadian beaver, another preparation comes from Russian animals, in particular Siberian beavers.

Canadian castor has an odor which, in dilution, resembles pine resin. Russian castor, on the other hand, has a leather-like odor, possibly due to a substance present in birch bark which is the staple food of Siberian beavers. Castor is used as a tincture or as an extract. It is a valuable fixative and is popular in imparting a spicy or Oriental note to perfumes.

Castoreum contains a complex mixture of about one hundred different substances, half of which have been identified.

Ambergris is a waxlike substance originating in the digestive tract of the sperm whale. The whale gives it off and since ambergris is lighter than water, it is found in the seas of tropical regions floating on the surface in yellow, grey, black or multicolored masses.

Ambergris is rare and therefore most expensive. The best ambergris is considered that which has been floating for years before it has been discovered. The odor of ambergris is extremely unpleasant when pure or concentrated, but it gives mellowness and permanency to mixtures. Like musk and civet, ambergris is a valuable fixative. Ambergris is used as an infusion in alcohol.

The most important constituent of ambergris is ambrein, a tricyclic triterpene alcohol. Oxidation of ambrien gives two series of strongly smelling substances: gamma-dihydroionone and its derivatives, and bicyclic substances derived from one, one, five, ten-tetramethyldecalin. Both of these series are now synthetically available,—the first from alpha-ionone, the second from scareol or the ionones.

The well-known aging process of the ambergris infusion is actually the through oxidative degradation of ambreine and of its primary decomposition product, ambreinolide. A tricyclic ketone produced by dehydration of ambreinolide also has a very persistent ambergris scent.

The greatest of care must be taken in the use of ambergris as a perfume component due to its strong animal note. Ambergris is used as an extract or tincture in de luxe perfumery. Ambergris tincture needs a very long time to mature, much longer than that of any other tincture of animal origin.

Among animal scents, musk has the greatest intensity, while ambergris has the highest durability of odor. K. Bergwein, therefore recommends ambergris for light flower perfumes, whereas perfumes with rather heavy notes will need the addition of musk or civet tincture.

Muskrat is the newest contribution to perfumery from animal sources. Chemically, the Musk Zibata is related to musk and civet. Its odor is powerful, lasting, musky and somewhat finer and less animal-like than musk-tonquin. It can be used either as a replacement for musk tonquin or as an addition product, to improve and exalt the quality of Asiatic musk. — W. Schweisheimer, *P. E. O. R* 47:56, 1956.

Compren (Eli Lilly and Company) is a high calcium phosphorus-free prenatal dietary supplement containing all major dietary supplemental factors found in clinical trials to be essential in pregnancy and lactation. The preparation is available in bottles of 100 and 500 capsules.

Trade Literature

Radioisotopes

A letter to the Oak Ridge National Laboratory, Union Carbide Nuclear Company, P. O. Box P, Oak Ridge, Tenn., will get you a revised Radioisotope Catalog. More than 100 different radioactive preparations made and distributed by the laboratory are listed with their respective specifications and price. Special sections are devoted to descriptions of the irradiation facilities in use, procedure for the procurement of isotopes, shipping information, special sources available, service or custom irradiations, neutron-activation analysis, and the laboratory's waste disposal service for users.

Flavors

Dodge & Olcott, Inc., 180 Varick Street, New York 14, has available a 68-page, spiral-bound, thumb-indexed, Reference Book and Catalog of Flavors and Seasonings. More than a year in preparation, this new book contains basic flavor information, including numerous formulas, tables, and a large reference chart for quick determination of the type of flavor to use for a wide range of products. The book is divided into fourteen sections, each tailored to a particular industry.

Epolene Waxes

Eastman Chemical Products, Kingsport, Tenn. has issued a 22-page brochure suggesting a wide range of possible applications for Epolene, a new line of polyethylene waxes. All the important physical properties of the two types of Epolene, emulsifiable (E designation) and non-emulsifiable (N designation), are listed along with comprehensive tables of their compatibility with other synthetic waxes, natural waxes, resins, and dye. Characterstic of Epolene-fortified paraffin are described in a series of graphs.

Odor Masking

Rhodia, Inc., 60 East 56th St., New York 22, has published a six-page brochure on the use of Alamask odor control chemicals for the abatement of obnoxious malodors in municipal and industrial sewage and waste treatment plants.

Stokes Equipment

F. J. Stokes Machine Company, 5500 Tabor Road, Philadelphia 20, has issued an eight-page bulletin describing the complete line of Stokes equipment for granulating, mixing and drying materials and for coating and polishing tablets. The equipment, developed as auxiliaries for Stokes tablet machines, is discussed in detail, and complete specifications are given.

Stokes has also issued a six-page bulletin describing two new rotary tablet machines, Model 533, with a maximum operating pressure of 10 tons, and Model 540, of four tons capacity. The bulletin illustrates and explains in detail a number of exclusive advanced design features which make for simplicity in setting up and adjusting their operation. These include grouping of all controls at the front of the press, locating feed frames where they can be seen from the operator's normal position, individual die screws, and hydraulic loading of the upper pressure roll with a single push-button control over the compacting pressure.

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(Continued from page 461)

Here was the first real demonstration that therapeutic agents could be used in the control of mental disease. Such a thought had occurred to many over the years, but the indications were very vague, and it appeared to be nothing more than a hunch. So little was thought of the idea that no company or research organization throughout the world was willing to back it with any money. But once the probable value of reserpine was indicated, the money poured forth and the chase was on.

The second of these tranquilizing drugs to become prominent also was originally intended for another use. Smith, Kline & French Laboratories' Thorazine (chlorpromazine) is a chemical of the antihistamine type developed in France. In fact it was first available in France under the name of Largactil for use in producing hypothermia in certain surgical procedures. When SKF first introduced it in this country it was recommended for control of nausea in pregnancy, and certain serious diseases. Its great value in control of mental disease was discovered later.

Frenquil (alpha-(4-piperidyl) benzhydrol hydrochloride) of The Wm. S. Merrell Company is one of the early products produced for the specific use of tranquilizing and thus controlling mental disorders. Miltown of Wallace Laboratories (Carter Products), and Equanil of Wyeth are both meprobromate, discovered by Wallace in research for just that type of product. Promazine, trademarked Sparine by Wyeth, is a newer one which is chlorpromazine (Thorazine) with the chlorine removed from the molecule. Pfizer's new Atarax is related to its antihistamine.

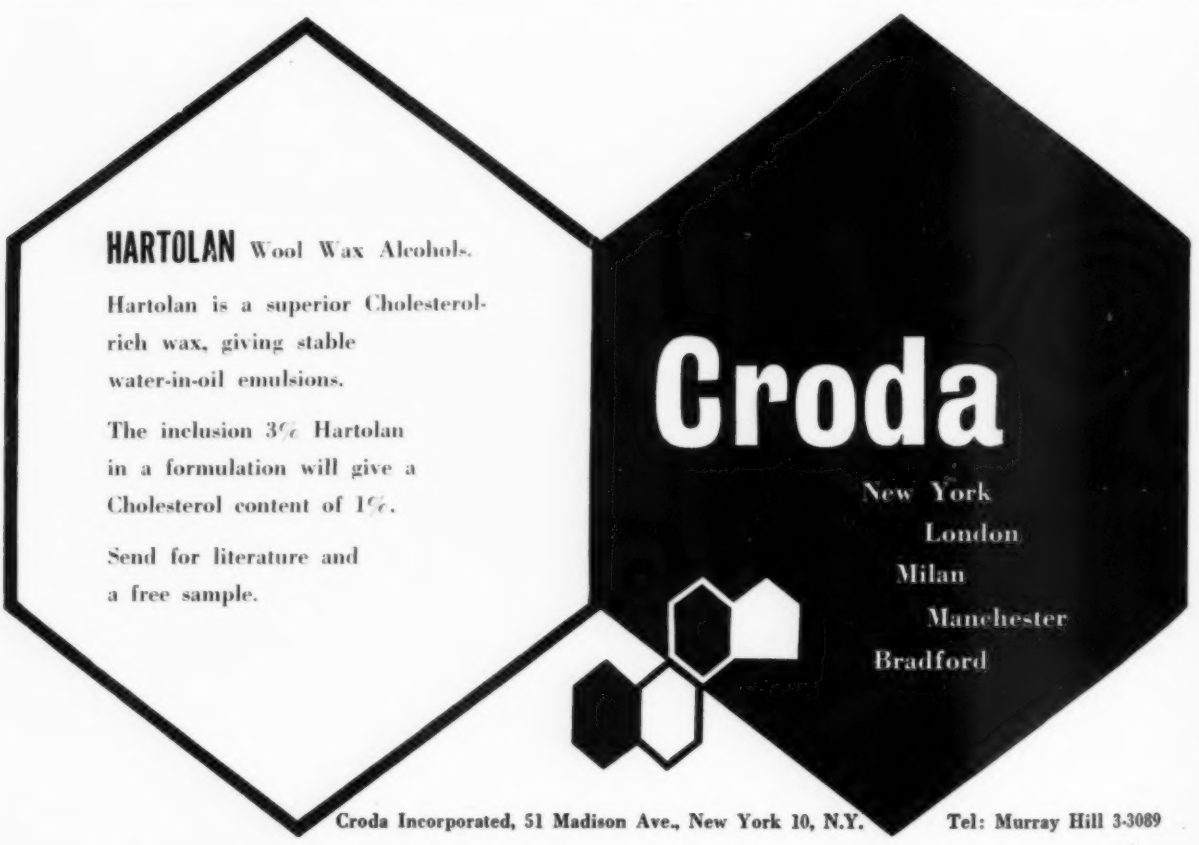
While the search goes on frantically for more and better drugs of this type, Dr. Frank M. Berger, medical director of Wallace Laboratories, points out that these tranquilizing drugs are effective only against the secondary symptoms of mental disease, such as anxiety, agitation and negativism, although they have "opened up new and unexpected vistas" in the treatment of the mentally ill. Furthermore, he maintains, the remarkable success achieved by these drugs in the control of mental patients underscores the belief that a misfunction of body chemistry, rather than emotional or organic factors may underlie some mental ills.

Dr. Berger recently stated that a drug that will strike at the underlying cause of mental disease rather than at the secondary symptoms, "may still be developed."

In recent experiments chemicals produced symptoms or conditions closely resembling mental illness, says Dr. Berger. Chemicals capable of producing these effects have been termed hallucinogens. The most potent of these, known as LSD, when given by mouth in small quantity, has produced a state similar to schizophrenia.

Every individual carries several potential halluci-

(Continued on page 550)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Industry's Books...

Essays in Biochemistry, *Samuel Graff, Editor, 345 pp., (1956), John Wiley & Sons, Inc., New York, cloth,* **$6.50.**

This work consisting of twenty-five essays, written in honor of Hans Thacher Clarke, survey the present status of biochemistry, discuss some major research problems, and speculate on future trends.

Androgens, Biochemistry, Physiology, and Clinical Significance, *by Ralph I. Dorfman, Ph.D., Associate Director of Laboratories, Worcester Foundation for Experimental Biology, and Reginald A. Shipley, M.D., Director, Radioisotope Unit Veterans Administration Hospital, 590 pp., John Wiley & Sons, Inc., New York, (1956), cloth,*

Drawing on all the information published in this field over the past 30 years, this book discusses the male hormones from both the theoretical and applied points of view. Especially valuable contributions are made by this book in the presentation of the clinical aspects of androgens. Clinical endocrinologists will find valuable information in the many uses of androgens in therapy and, at the same time, gain an understanding of the fundamental research that supports the clinical applications. The structural variations of the steroid molecule are discussed and a structural formula is included for each steroid mentioned. Also included is a unique compendium of the world's literature on 17-ketosteroids in health and disease.

Drug Store Operating Costs and Profits, *Orin E. Burley, Director of Project, Director of Research, the National Wholesale Druggists' Association, and Robert G. Cox, Cost Supervisor, Assistant Professor of Accounting, Wharton School of Finance and Commerce University of Pennsylvania, 549 pp., Illus., McGraw-Hill Book Co., New York, (1956), cloth* **$8.50**

Here are practical ways to measure, and effectively control drug store operating costs—get a true picture of margins and sales—and eliminate hidden losses. In addition, the book provides data on a wide variety of actual store operations, enabling the reader to draw upon the experience of others. With these techniques and data, policies for profitable merchandising at lower operating costs may be planned more intelligently. The book shows how to determine which departments and commodities in the store are making money—which are draining away profits. It helps decide where sales and merchandising efforts should be increased—and where they are being wasted on low-profit, slow-moving items.

Chemical Safety Supervision, *by Joseph Guelich, Safety Manager General Chemical Div., Allied Chemical and Dye Corp., 221 pp., Reinhold Publishing Corp., New York, (1956), cloth,* **$4.50.**

This is a handbook of safety for everyone who manufactures, handles or uses chemicals. Designed primarily for supervisors and foremen, it shows in simple style how to cut down on carelessness and develop safe handling habits among employees. Full chapters explain tested, proven methods of teaching the use of chemicals to new men, protecting men from hazards, moving and storing chemicals, first aid, scheduling physical examinations, and many other safety concepts.

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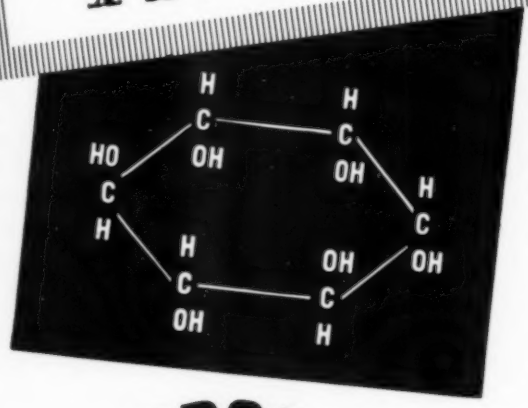

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(*Continued from page 548*)

nogens within him, Dr. Berger said, among which adrenaline "is perhaps the most interesting." When adrenaline is given by injection, he said, intense anxiety often develops. This may be due to the adrenaline itself, or to a breakdown product of adrenaline. This suggests that mental disease may be caused by an error in adrenaline metabolism.

Certain studies point up the possibility that mental disease may be traced to either an excess or deficiency in the brain of another body chemical, serotonin, a substance which resembles the hallucinogens and which is apparently affected by them in two ways. Hallucinogens have been found to destroy the potency of serotonin, Dr. Berger explained, thereby creating, in effect, a deficiency; and they have also been shown to retard the work of the enzymes which help keep the supply of serotonin at a normal level. This may result in an excess of serotonin in the brain.

One of the tranquilizers, reserpine, has been found to reduce the serotonin level in the brain, again suggesting a link with mental diseases. Another tranquilizer, chloropromazine, tends to limit the action of the hallucinogen adrenaline, Dr. Berger pointed out, again indicating a chemical basis for mental illness. A third tranquilizer, meprobamate, however, acts in an entirely different manner, according to Dr. Berger, with no effect on either serotonin or adrenaline. Meprobamate acts on the thalamus, a group of nerve cells in the brain concerned with sensations, emotions and social behavior, and appears to control anxiety itself, rather than merely the symptoms of anxiety.

RAUWOLFIA AND ITS ALKALOIDS

(*Continued from page 466*)

difference. This is where the botanists begin to have their differences of opinion and interpretation.

From the point of view of most botanists, thenames of four species of *Rauwolfia* should be consolidated into one. *Rauwolfia tetraphylla L.* is the correct name for the various drug sources currently employed under the names *R. canescens*, *R. heterophylla* and *R. hirsuta*.

It is thought that *Rauwolfia tetraphylla L.* originally came from the Caribbean area, but it is not known whether it first occurred on the mainland of Central America or on one of the islands of the Caribbean. Sometime in the 17th century the plant was introduced into India and now it has spread up and down the eastern coast of India and in the northeastern portion, in Bengal.

But in addition to the botanists, the chemists have their say. For some reason known only to mother nature, the *Rauwolfia* commonly referred to as *Rauwolfia canescens*, is of somewhat different chemical makeup from that of *Rauwolfia tetraphylla* of the Caribbean and Central American areas. *R. canescens*, alone of these, contains raunormine.

It having been demonstrated that there are quite

distinct chemical differences between *Rauwolfia canescens* root and *Rauwolfia tetraphylla* root, it is suggested that there are good and sufficient practical reasons for the drug industry to differentiate between these two basic kinds of root—*R. canescens* of India, and *R. tetraphylla* (*R. hirsuta* or *R. heterophylla*) of Central America.

III. Reserpine

Sources of Reserpine

There are five species of *Rauwolfia* which have been used in the production of reserpine in commercial quantities:

R. serpentina
R. canescens
R. micrantha
R. tetraphylla (hirsuta or heterophylla)
R. vomitoria

So far as quantity is concerned, *R. vomitoria* and *R. tetraphylla* have been the leaders.

So far as quality is concerned, any of these species can be made to yield products of exceptional purity, but each source presents certain problems. For example in *R. serpentina* the rescinnamine behaves much like the reserpine throughout the extraction process, in fact, one assay procedure for *R. serpentina* suggested by the government ends up with these two alkaloids being measured together. With *R. canescens* the problem is to separate the raunormine. With *R. vomitoria* the problem is to separate the reserpine from the resins.

Fortunately, reserpine has been very thoroughly characterized and is commercially available in a very acceptable state of purity.

Supplies of Reserpine

Because of the varied sources of crude root usable for the manufacture of reserpine, and because these crudes are widely distributed in quite some abundance in both the Eastern and Western hemisphere there is little need to become concerned about any eventual shortage of reserpine. Certainly there is enough root for reserpine to last another ten years.

And other species of *Rauwolfia* are being investigated all the time; already over thirty have been checked. Some species of *Rauwolfia* are very high in total alkaloids—but are not usable; for example, one species has over 6.0 per cent of total alkaloids (three times as much as *R. serpentina*) but the reserpine content was found to be nil. Another factor to consider is the utility of other alkaloids of *Rauwolfia* roots yielding reserpine. The more alkaloids put to profitable use from any one specie, the lower the price of the various products, especially the reserpine.

But in order to be on the safe side, a number of laboratories are working on the possible complete synthesis of the reserpine. Other laboratories are working on related alkaloids obtainable from other species of plants, particularly plants related to *Rau-*

(Continued on page 563)

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(*Continued from page 503*)

of the fine fabric flakes, to incorporate at least 10 but not over 30 per cent by weight potassium soaps to improve the solubility of the sodium soaps, and to decrease the brittleness of the chips.

In the production of soaps, and in particular solid soaps, the main fat employed is tallow, while coconut oil is also extensively used. Tallow is a much less expensive raw material than coconut oil, and therefore it would be desired to use tallow exclusively, if it were possible to do so and obtain a satisfactory product. However, it has been found necessary to combine between 10 and 35 per cent by weight coconut oil soaps with the tallow soaps to enhance the solubility and sudsing characteristics of the tallow base soaps.

Potassium soaps are commonly referred to as soft soaps, because of their great affinity for water, and because they are prepared and marketed in the form of liquid or paste soap products, rather than in the form of hard soaps. For example, liquid soaps for use in dispensers are usually made from coconut oil using 100 per cent caustic potash saponification. So-called "green soaps" are paste products made with soft oils or fatty acids and 100 per cent caustic potash saponification. Shaving creams usually contain substantial percentages of coconut oil and hard fats or fatty acids saponified with caustic potash. With the exception of soap flakes or chips, mentioned above, hard soap products are not formulated with any potassium soaps, and even in the case of soap chips only a minor proportion of potassium soaps are combined with the sodium soaps.

Probably the primary reason for the failure of the soap industry to market potassium base soaps in solid form is due to their hygroscopicity. This defect of potassium soaps has long been recognized. They have a much greater affinity for water than sodium soaps, and tend to take up water from the atmosphere when exposed thereto. Also, in bar form, potassium soaps tend to soften excessively on contact with water. When potassium soaps are prepared in the form of chips or granules, the greater area of exposed surface accentuates the effect of the hygroscopic tendency of the soap. However, aside from this defect, the potassium soaps have desirable properties which are comparable to and in some ways superior to sodium soaps. For example, potassium soaps go into aqueous solution at much lower temperatures than sodium soaps.

The Armour invention is based on the discovery that by reducing the moisture content of solid potassium face soaps below a critical value (at least four per cent) the objectionable hydroscopic tendency of the soap is substantially eliminated, with the result that when potassium soap is dried below this limit it can be marketed in any desired form, such as bars, chips, and granules.

Heretofore, the patent points out, it has been the practice to prepare solid soap products with a high

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percentage of water. For example, toilet soap in bar form and washing soap in granule form contain between 10 to 15 per cent moisture; soap in the form of chips contains between 10 to 20 per cent moisture; and laundry soap in bar form contains up to 30 per cent of moisture. The patent points out that in general solid soaps must contain at least about 10 per cent of water to give satisfactory results in both manufacturing and commercial use. This amount of water is required in the soap during processing to allow the milling operations to be carried out without hardening and powdering the soaps. Also, if the finished product contains less than about 10 per cent water, it would not be sufficiently soluble to give satisfactory results under ordinary conditions of use.

The potassium soaps of the invention are made with the same equipment now used for preparing solid sodium soaps, with some variations in the procedure.

An important economic advantage resulting from the invention is that potassium soaps prepared exclusively from cheaper tallow fatty acids are said to have properties which are substantially the equivalent of the ordinary commercial grades of sodium soaps which are tallow based soaps but which in addition contain from 10 to 30 per cent of the more expensive coconut oil soap.

The Armour inventors found that in addition to the moisture factor there is another factor which has some effect on the hygroscopicity of the potassium soaps. This factor is the titer of the fatty raw material. The patent defines titer as a standard test for fats and oils in which the sample is completely saponified, and the solidifying point (or titer) of the resulting separated and washed fatty acids are determined. In preparing solid potassium soaps from tallow, it has been determined that when the tallow has a relatively high titer the hygroscopic tendency of the finished soap is somewhat reduced. The titer of tallow or other fat can be increased by hydrogenation, if its titer is lower than desirable. Also, a mixture having the desired titer can be prepared by the mixing of a low titer stock with a high titer stock. Generally in the manufacturing of sodium soaps, the titer of the tallow is not regarded of particular importance. In preparing solid potassium soaps from tallow, it is desirable to have the titer of the tallow at least 40° C. and preferably at least 43° C. Completely hardened tallow is undesirable, and it is probable that it will not be desirable to use tallow having a titer much above 50° C. The optimum range is from about 43 to 47° C.

CORRECTION:

The illustration on page 173 of our February issue was incorrectly credited to Germaine Monteil. Credit should have been given to Rilling Dermetics Company who kindly furnished us with the photograph.

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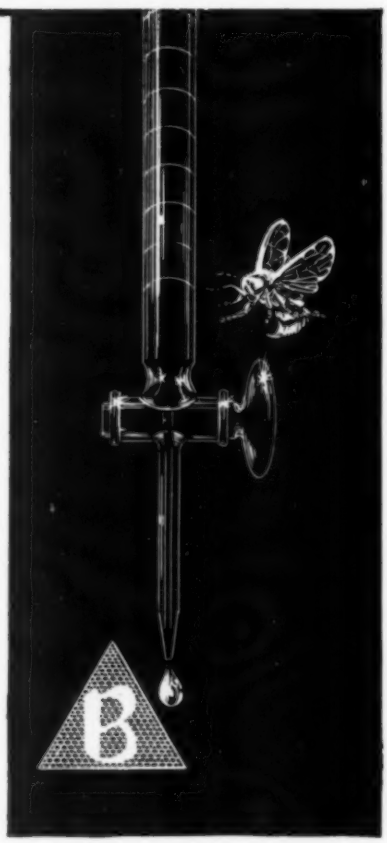

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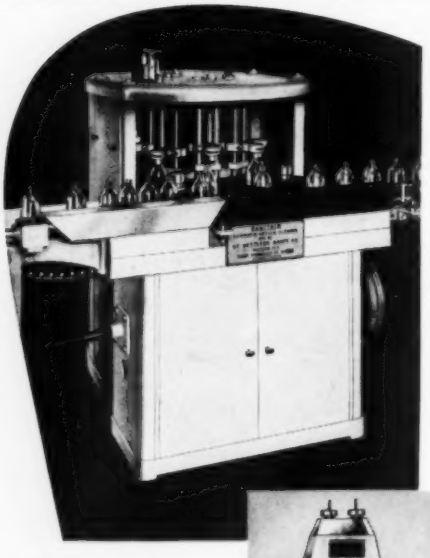
(Continued from page 476)

embodied the formula of "Rise" in combination with a formula which Colgate had theretofore not found successful. He gave Colgate, also, the benefit of knowledge obtained at Snell's with respect to improving the "Rise" formula by superfatting so as to produce a smoother lather and one which gives the feeling on the skin produced by the so-called brushless shaving creams. Colgate had Fine to file applications for patents covering this improved lather. Notwithstanding this experience and attempts to obtain patents in its own behalf on the subject matter, Colgate argues that the patent here in suit is lacking in invention and is anticipated by both domestic and foreign patents and by prior use.

The three domestic patents relied on as anticipations were all considered by the Patent Office before granting the patent. They are Rotheim No. 1,892,750 of 1937, Getz No. 2,294,172 of 1948 and Boe No. 2,524,590 of 1950. We agree with the trial judge that none of these anticipates and that taken together they do not negative invention in the patent in suit. Rotheim relates to a method of atomizing materials of a liquid or semi-liquid consistency. Liquid soap is given as one of the materials that may be atomized. No Freons are listed as propellants. Getz is a patent for aerating food products such as whipped cream, where a solution and not an emulsion is what is desired. Its only possible relevancy is that it lists among the propellants Freon-12, which has long been used as a propellant of insecticides. Boe relates to spraying. While it lists Freons, among other gases, as propellants and suggests that the gases listed may be mixed to arrive at a desirable vapor pressure, it does not specify which gases. It does not suggest the creation of a lather, but points out how foaming may be prevented.

Foreign patents relied on by defendants were the Belgian Patent to Estignard-Bluard of 1949 and Argentine and Panama patents to Daggett & Ramsdell of 1946. These patents were excluded on legal grounds by the trial court, the Belgian patent on the ground that although the patent was granted by decree prior to the conception date of the invention involved in the patent in suit, it was not opened to the public until after that date, the Argentine and Panama patents on the ground that only the claims of the patent could be considered and these were irrelevant. Assuming without deciding that there was error in the exclusion of these patents, the position of defendants is not helped, since neither of these teaches how to produce the pressurized shaving cream of the patent in suit. The Belgian patent relates to the formation of pressurized gaseous emulsions and lists a large number of gaseous propellants, but not including Freon-114, with all sorts of liquids to be used therewith including soaps as emulsifying agents only. It suggests the problem of developing a pressurized shaving cream but does not teach which of the propellants should be used for that purpose or with what combination of soaps



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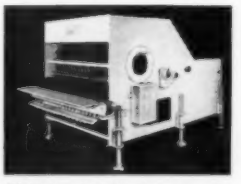

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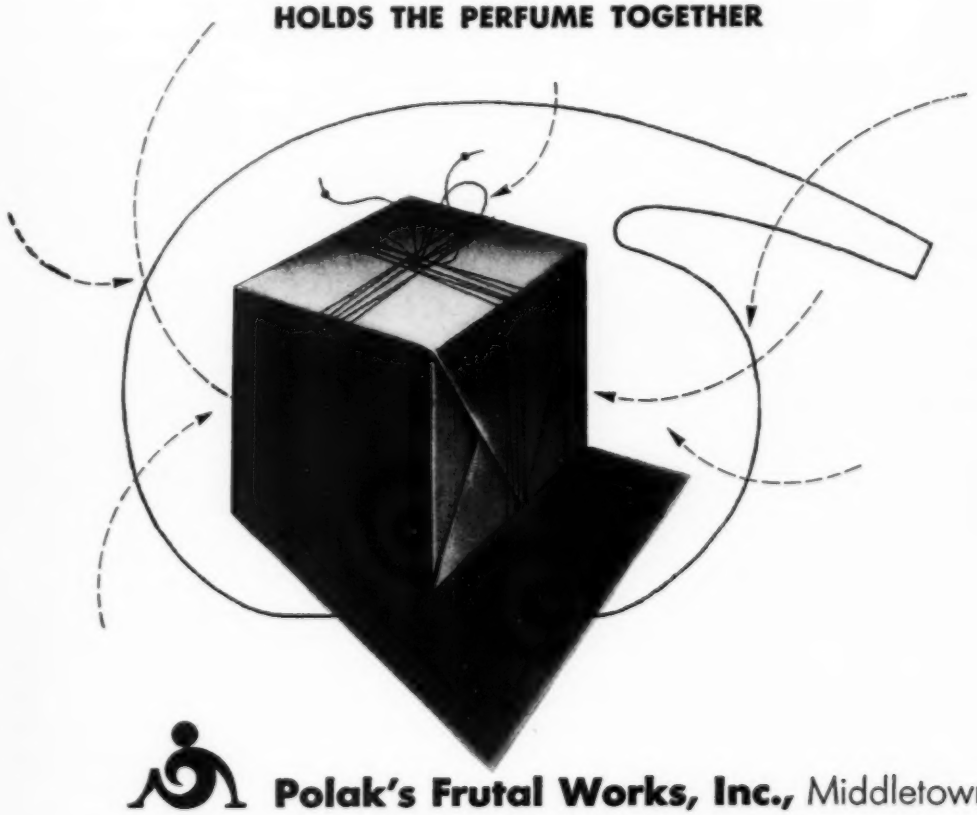

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they should be used. The Argentine and Panama patents relate to spraying cosmetics and, while formulas for shaving creams are included among the cosmetics to be sprayed, none of these formulas would aid in solving the problem which was solved by the patent in suit. They merely list "propellants" without indicating what mixture of propellants is to be used with what mixture of soaps.

Defendants rely upon prior use by Gebauer and Segelken. Gebauer developed a shampoo which jelled and which used Freon-11 as a propellant. It manifestly did not anticipate nor suggest the pressurized shaving cream of the patent. Segelken was the chemist employed by Daggett-Ramsdell upon whose experiments the Argentine and Panama patents were obtained. While he testifies that in the course of his experiments he produced a satisfactory pressurized shaving cream, it is not shown that he used the combination either of propellants or soaps prescribed by the patent or that he eliminated objectionable matters eliminated by that combination or achieved the results obtained by it. The evidence relied upon falls far short of the sort of evidence necessary to invalidate a patent by oral evidence of prior use. See the *Barbed Wire Patent*, 143 U. S. 275, 284; *Adamson* v. *Gilliland*, 242 U. S. 350; *Hoeltke* v. *C. M. Kemp Mfg. Co.*, 4 Cir. 80 F. 2d 912, 923.

The real question as to the validity of the patent is not one of anticipation or of prior use but of invention. The question is whether the product of the patent is mere aggregation, in which old elements accomplish independently what they did in the prior art, or whether there is a true combination in which old elements have been combined to produce a new and useful result. We think that the latter is the case. What we have is not the mere use of propellant gases to extrude shaving soap from a container. But the use of particular propellant gases liquefied under pressure and combined in such way with particular aqueous soap solutions as to produce an emulsion, which, when released from the container, becomes a lather composed of tiny gas bubbles coated with soap and useful for shaving—a product which was new and useful, which the expert chemists of Colgate had tried unsuccessfully to produce, and which achieved at once unqualified commercial success.

A sufficient answer to the argument that nothing more is involved than the skill of the art is that the patentees experimented for months in the effort to produce the pressurized shaving cream of the patent before their efforts finally resulted in success, that Colgate's efforts to produce it proved unsuccessful and that, after it had been produced and Colgate had purchased it on the market and had it analyzed, Colgate's corps of expert chemists were still not able to produce it until the knowledge of one of the patentees was availed of. As said by Mr. Justice McKenna in the Grant Tire case, *Consolidated Rubber Co.* v. *Consolidated Tire Co.* 220 U. S. 428, 435, "Knowledge after the event is always easy, and problems once

solved present no difficulties, indeed, may be represented as never having had any, and expert witnesses may be brought forward to show that the new thing which seemed to have eluded the search of the world was always ready at hand and easy to be seen by a merely skillful attention. But the law has other tests of the invention than subtle conjectures of what might have been seen and yet was not. It regards a change as evidence of novelty, the acceptance and utility of change as a further evidence, even as demonstration."

That the product of the patent is a true combination and not a mere aggregation clearly follows from the application of the principles approved and applied by this court in the Canned Heat Patent case, which is very much in point here. *United States Industrial Chemical Co.* v. *Theroz Co.*, 4 Cir. 25 F. 2d 387. In that case we quoted with approval the following passage from 20 R. C. L. 1125-1126, which we understand to be a correct statement of the principles of law here applicable, viz.:

> "A combination is a composition of elements, some of which may be old and others new, or all old or all new. It is, however, the combination that is the invention, and is as much a unit in contemplation of law as a single or noncomposite instrument. The authorities establish the following propositions respecting the patentability of devices or processes of this character: (1) That a combination is patentable if it produces new and useful results, though all its constituents were well known and in common use before it was made, provided the results are a product of the combination, and not a mere aggregate of several results, each the product of one of the combined elements. (2) If it produces a different force, effect, or result in the combined forces or processes from that given by their separate parts, and a new result is given by their union. (3) If it either forms a new machine of distinct character or formation, or produces a result which is not the mere aggregate of separate contributions, but is due to the joint and cooperating action of all the elements. (4) When the several elements of which it is composed produce by their joint action either a new and useful result, or an old result in a cheaper or otherwise more advantageous way".

The patentability of "Rise" is supported by every criterion here laid down. First it produces a new and useful result, and this result is a product of the combination, and not the mere aggregate of several results; second, it produces a different result in the combined forces or processes from that given by their separate parts, and a new result is given by their union; third, it produces a result which is not the mere aggregate of separate contributions, but is due to the joint and cooperating action of all the elements; and, fourth, the several elements of which the product is composed

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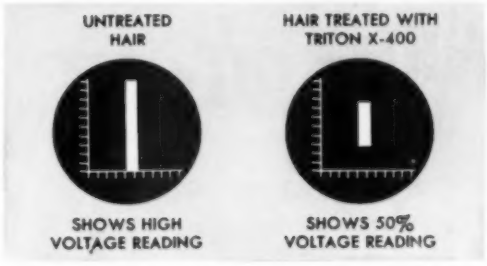

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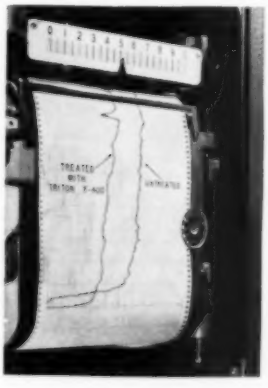

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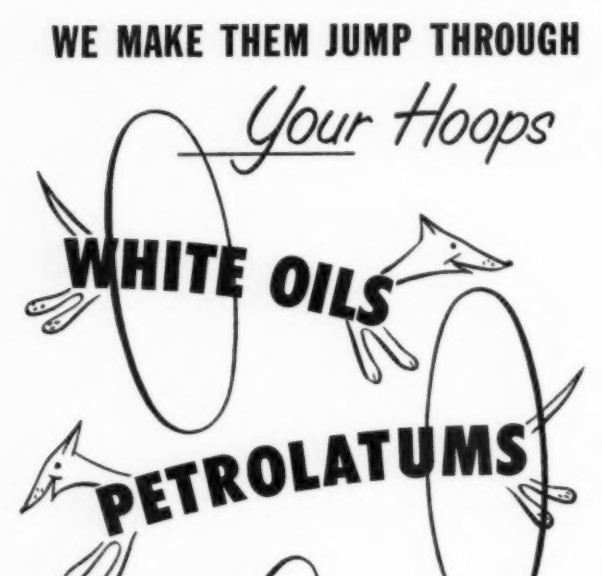

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The case presented is thus fundamentally different from *Mandel Bros.* v. *Wallace*, 335 U. S. 291, where all that was done was to use a drug with a cosmetic preparation to accomplish a purpose for which its availability had long been known and recognized. What we have here is a new and useful composition of matter produced after lengthy experimentation, in which the various elements combine to produce a new and useful result. To the presumption that the finding of the District Judge as to validity is correct, a finding based upon lengthy evidence and the testimony of experts (see *Graver Tank & Mfg. Co.* v. *Linde Air Products Co.*, 336 U. S. 271), must be added the presumptions of validity arising from the fact that the patent was issued by the Patent Office, from the fact that the patented product entered at once into wide public use and achieved outstanding commercial success, and from the fact that it was copied by an infringer who was one of the largest soap manufacturers of the country and who had been trying in vain to develop a similar product but had been unable to do so until the knowledge of one of the patentees was obtained.

2. *The Trade Secrets.*

The District Judge made the following finding as to misappropriation of trade secrets by Colgate, viz.:

> "12. That the defendant Colgate-Palmolive Company has wrongfully and unlawfully misappropriated trade secrets of plaintiff by embodying them in pressurized lather shaving compositions as follows:
>
> "(a) By combining the trade secret of the formula of the soap solution in the plaintiffs' product 'Rise' with diluted Colgate lather cream to make 'Rapid Shave No. 1.'
>
> "(b) By employing in some containers of 'Rapid Shave No. 1' plaintiffs' trade secret in the heat annealing process for polyethylene siphon tubes.
>
> "(c) By combining in a pressurized lather-generating composition a soap solution superfatted with petrolatum, carbowax and excess stearic acid, and embodying said secret combination in its products 'Rapid Shave No. 2' and 'Instant Barber Shave.'
>
> "The above-described trade secret of sub-paragraph (c) was not disclosed or claimed in plaintiffs' United States Letters Patent No. 2,655,480, in suit."

In his opinion the District Judge set forth the facts and chronology upon which the foregoing findings were based as follows:

> "We find to be correct, by the weight of the credible evidence, the following chronology of what occurred from the beginning of the development of 'Rise' to the institution of the present suit: March 1, 1949: Spitzer, Reich and Fine began their research and development work. April, 1950: Carter put 'Rise' on the market. May and July, 1950: Colgate analyzed 'Rise,' and endeavored, unsuccessfully, to duplicate it, although

claiming that the 'Rise' formula had been completely reproduced but was not found satisfactory, particularly because it did not result in sufficient exhaustion of the product from the can. Also, Colgate was troubled with sputtering of the product. September, 1950: Fine entered the employment of Colgate although he had been a co-inventor of 'Rise.' October, 1950: Fine revealed to Colgate the causes of the sputtering. November, 1950: Fine disclosed to Colgate the precise formula of 'Rise,' and also combined that formula with diluted Colgate lather, to make Rapid-Shave No. 1. Further, he disclosed to Colgate, and to the latter's supplier of valves, the siphon tube annealing process employed by Carter for 'Rise.' August, 1951: Colgate filed in Fine's name a patent application covering the formula of Rapid-Shave No. 1, which embodied his work originally done on 'Rise.' November, 1951: Fine prepared, and disclosed to Hansen, his assistant at Colgate, a duplicate formula for 'Rise,' superfatted, i.e., with excess of fatty matter (soap). September, 1952, until February, 1953: Colgate pursued its experimentation in superfatting the 'Rise' formula with petrolatum, carbowax and excess stearic acid, and then marketed its Rapid-Shave No. 2. September 1953: Colgate filed its second patent application in the name of Fine and associates, based on the development work that Fine had done while employed by Snell."

We agree with the District Judge that Colgate must be held to liability for the appropriation and use of the "Rise" formula in developing its shaving cream. That formula had been developed in the confidential work of Snell for Spitzer. Fine as an employee of Snell was under contract with Snell not to disclose information obtained in the course of this work. Colgate knew of Fine's employment and of his work on the development of "Rise," which Colgate had been unable to produce even after purchasing it on the market and having it analyzed. Although Colgate had twice before this refused to employ Fine, and although it knew of the confidential nature of his employment with Snell, it proceeded to employ him while it was engaged in the effort to develop a pressurized shaving cream and, within a month of his employment, put him to work on the problem, which he solved immediately by using the "Rise" formula in combination with a formula which Colgate had found unsuccessful.

With respect to the superfatting, it appears that this was worked out at Snell's to give the lather a "brushless effect" after the patent in suit had been applied for. It also appears that Fine, who had developed the superfatting process in the course of his work at Snell's, suggested it to Colgate and that Colgate adopted the process and caused an application for a patent covering it to be filed by Fine.

On these facts, there can be no question but that

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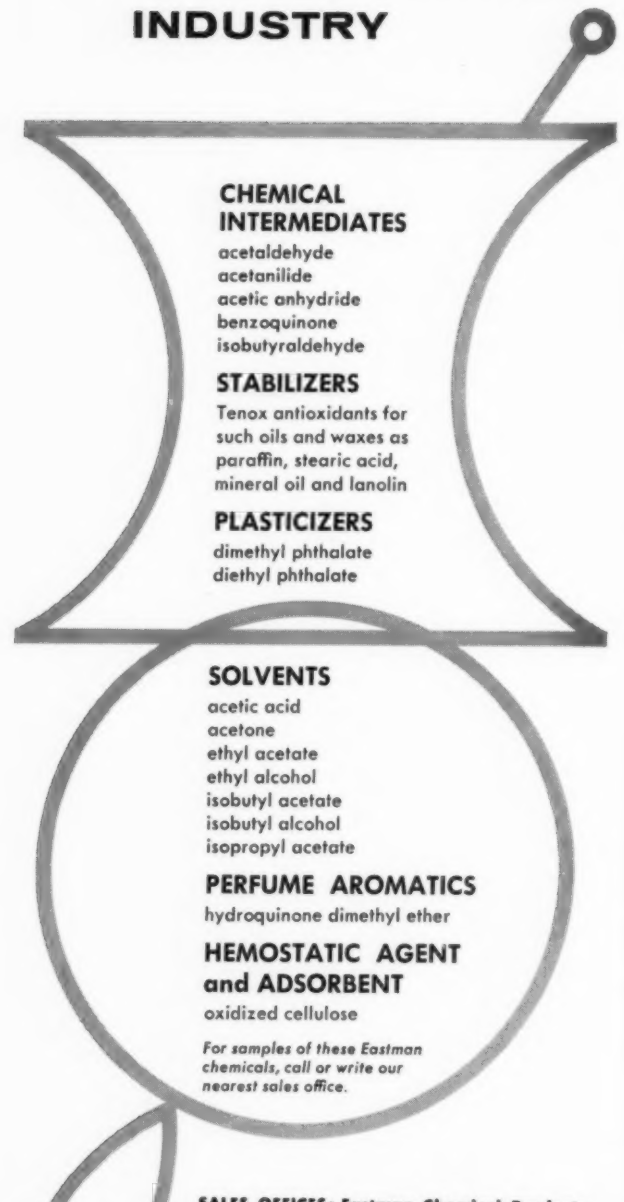

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Colgate used the knowledge of Fine in producing its pressurized shaving cream or that this knowledge related to matters which were trade secrets of Spitzer and his associates. That Colgate did not enter into an open bargain with Fine to disclose this confidential information is no defense. Nor is it a defense that Fine upon his employment was entitled to use his skill in Colgate's interest. He was not entitled to give to Colgate the benefit of business secrets which had been disclosed to him at Snell's; and Colgate could not close its eyes to facts which clearly indicated that this was what he was doing, even if he had not been employed for that express purpose. One may not escape liability for appropriating the business secrets of another by employing one who has been entrusted with the secrets and permitting him to make use of them. With respect to this the District Judge said:

> "* * * it is not necessary to, nor do we find that Colgate's employment of Fine was originally arranged for the specific purpose of having him divulge confidential information about the 'Rise' patent that he had acquired at Snell's. The basis of our decision that Colgate's action was wrongful is that Colgate knew, or must have known by the exercise of fair business principles, that the precise character of Fine's work with Snell was, in all likelihood, covered by the agreement which Fine had with Snell not to divulge trade secrets, and that, therefore, Colgate was obligated to do more than it did towards ascertaining the extent to which Fine was, in fact, restricted in what he might disclose to Colgate. That it was wrong for Colgate not to go further than it did in this respect is confirmed by the very status of Fine when he came to Colgate. At that time Fine was a joint inventor and patentee of 'Rise.' In other words, Fine was willing to be, and was knowingly placed by Colgate in work that was in direct competition with the work in which Fine had shared at Snell's, resulting, ultimately in his own patent. The very fact that Fine would do this should, per se, have raised in the minds of the representatives of Colgate, who arranged the employment of Fine, a feeling that he was entering upon a rather strange employment under the circumstances. It, therefore, was not enough for Colgate to say that they would see that Fine lived up to the limitations imposed by his contract with Snell. The weight of the credible evidence discloses that Colgate was far from being sufficiently avid to ascertain what those limitations really were, and to have Fine live up to them."

The principles of law applicable are well settled and are well stated in section 757 of the A.L.I. Restatement of Torts as follows:

> "One who discloses or uses another's trade secret, without a privilege to do so, is liable to the other if
>
> * * *
>
> "(c) he learned the secret from a third person

with notice of the facts that it was a secret and that the third person discovered it by improper means or that the third person's disclosure of it was otherwise a breach of his duty to the other, * * *."

Directly in point in support of the proposition thus stated are *Peabody* v. *Norfolk*, 98 *Mass.* 452, 96 Am. Dec. 664 (opinion by Gray, J.); *Nulomoline* v. *Stromeyer*, 3 Cir. 249 F. 597; *Herold* v. *Herold China & Pottery Co.*, 6 Cir. 257 F. 911; *A. O. Smith Corp.* v. *Petroleum Iron Works of Ohio*, 6 Cir. 73 F. 2d 531, 539; *Ferroline Corp.* v. *General Aniline & Film Corp.*, 7 Cir. 207 F. 2d 912, 921; *Seismograph Service Corp.* v. *Offshore Raydist* (E.D.La.), 135 F. Supp. 342, 354; *Lamont C. & Co.* v. *Bonnie Blend Chocolate Corp.*, 238 N. Y. S. 78. See also *Smith* v. *Dravo Corp?*. 7 Cir. 203 F. 2d 369, 375; *Franke* v. *Wiltschek*, 2 Cir. 209 F. 2d 493, 495. *Nulomoline* v. *Stromeyer*, *supra*, was a case in which the appropriation of the trade secret resulted, as here, from the employment of one to whom it had been imparted in the course of a former employment. In *Herold* v. *Herold China & Pottery Co.*, *supra*, Judge Knappen, speaking for the Court of Appeals of the Sixth Circuit, stated the rule as follows:

> "The rule is well settled that secret formulas and processes, such as are claimed to be involved here, are property rights which will be protected by injunction, not only as against those who attempt to disclose or use them in violation of confidential relations or contracts express or implied, but as against those who are participating in such attempt with knowledge of such confidential relations or contract, though they might in time have reached the same result by their own independent experiments or efforts."

We do not think that the finding, 12(b), with respect to the annealing of the polyethylene tubes by dipping them in hot water can be sustained. While Fine learned of this at Snell's and communicated his knowledge to Colgate, the process was one which was well known and cannot be treated as a trade secret or a confidential disclosure. *American Potato Dryers* v. *Peters*, 4 Cir. 184 F. 2d 165, 172; A.L.I. Restatement of Torts, sec. 757, Comment (b), pp. 5-6. This, however, is not material since no injunctive relief is granted with respect thereto and the damages, whether based on the use of the original "Rise" formula or the superfatted formula, would not be affected thereby.

3. *The Decree.*

Decree was properly entered enjoining infringement of the patent and awarding damages because of infringement, and, as to Colgate, awarding damages from the time that this defendant began using the trade secrets which it has obtained by the employment of Fine. *Hoeltke* v. *Kemp Mfg. Co.*, 4 Cir. 80 F. 2d 912, 922, 923; *C. & O. R. Co.* v. *Kaltenback*, 4 Cir. 95 F. 2d 801, 806; *Ackerman* v. *General Motors Corp.*, 4 Cir. 202 F. 2d 642, 645. The decree properly ordered that all rights under the patent applications filed by

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Fine at Colgate's direction be assigned to plaintiffs. Without intimating any opinion as to whether patent should issue on these applications, we think it clear that, if patents should issue, all rights therein, in equity and good conscience, belong to plaintiffs, since the discovery or invention involved was made by Fine while employed for the purpose of making it. *Standard Parts Co.* v. *Peck*, 264 U. S. 52; *Becher* v. *Conture Laboratories*, 279 U. S. 388; *Houghton* v. *United States*, 4 Cir. 23 F. 2d 386, 388; *Saco Lowell Shops* v. *Reynolds*, 4 Cir. 141 F. 2d 587; *Reynolds* v. *Whitin Machine Works*, 4 Cir. 167 F. 2d 78, 86; *Shellmar Products Co.* v. *Allen-Qualley Co.*, 7 Cir. 36 F. 2d 623.

Question is raised as to the awarding of attorneys' fees against Colgate under 35 USC 285: but this was a matter resting in the sound discretion of the trial court and we cannot say that the discretion was abused. *Orrison* v. *C. Hoffberger Co.*, 4 Cir. 190 F. 2d 787, 791; *Aeration Processes Inc.* v. *Walter Kidde & Co.*, 2 Cir. 177 F. 2d 772; *Pacific Contact Laboratories* v. *Solex Laboratories*, 9 Cir. 209 F. 2d 529, 533. This is not an ordinary case of infringement. It is a case of deliberate and wilful infringement based upon and made possible by appropriation of trade secrets upon the basis of which Colgate has itself attempted to obtain a patent. The court below has termed the defense "specious." Whether "specious" or not, the circumstances were certainly sufficient to make this an "exceptional" case within the meaning of the statute, the purpose of which was to give the court power to throw the burden of unnecessary and vexatious litigation on the shoulders of those who are responsible for it.

Other questions raised by the appeal warrant but scant mention. It is urged that there was error in refusing to require plaintiffs to furnish to defendants the correspondence passing between plaintiffs' agents and counsel with reference to the Rotheim patent when it was being considered by the Patent Office in connection with the patent in suit. The motion was denied on the ground that it involved privileged communications of counsel, but the correspondence was proffered for examination by the court. Aside from the question of privilege, it is a matter resting in the discretion of the court as to how far parties should be allowed to go in a fishing expedition of this sort; and there is nothing to show that the discretion was abused or that there was anything in connection with this correspondence which would warrant our sending the case back for rehearing. The same may be said as to the action of the court in holding the parties to the trial of the issues involved in the case and in excluding evidence offered with respect to the use of propellants in the art relating to insecticides. Complaint is made that the trial judge was impatient with counsel, but an examination of the record shows that he tried the case carefully and with a great deal more patience than most judges would have exercised

under similar circumstances. He gave six weeks to a case which should have been tried in a much shorter period, and at its conclusion counsel for defendants expressed their appreciation of the patience which he had exhibited throughout the trial.

The decree appealed from will be affirmed.

Affirmed.

RAUWOLFIA AND ITS ALKALOIDS

(Continued from page 551)

wolfia. One such genus is *Alstonia* from Australia. Another is Yohimbi bark from Africa. In both instances the percentages of alkaloids is comparatively low, the cost of the crude is relatively high, and the plants are not nearly as abundant as *Rauwolfia.* This does not mean that the search should be discontinued, by any means. It is quite possible that alkaloids will be located in related plants—alkaloids that could be chemically transformed into reserpine, or into compounds related to reserpine, which might be even of greater value to medicine.

IV. Other Rauwolfia Alkaloids and Preparations

Other than whole *R. serpentina* and reserpine, there are products in use based on selected groups of *Rauwolfia* alkaloids. The total mixed alkaloids of *R. serpentina* have been used in India, and offered to this country, but the precise constitution has been uncertain and has varied.

The next step is a selection of alkaloids, a selection based on rather elementary chemical properties. On this basis there are three categories of *Rauwolfia* alkaloids and in particular, of the alkaloids of *R. serpentina:*

Weakly basic (including reserpine)
Moderately basic
Strongly basic

With some further selection beyond these groups, but short of obtaining a single pure alkaloid, certain other pharmaceutical preparations are derived.

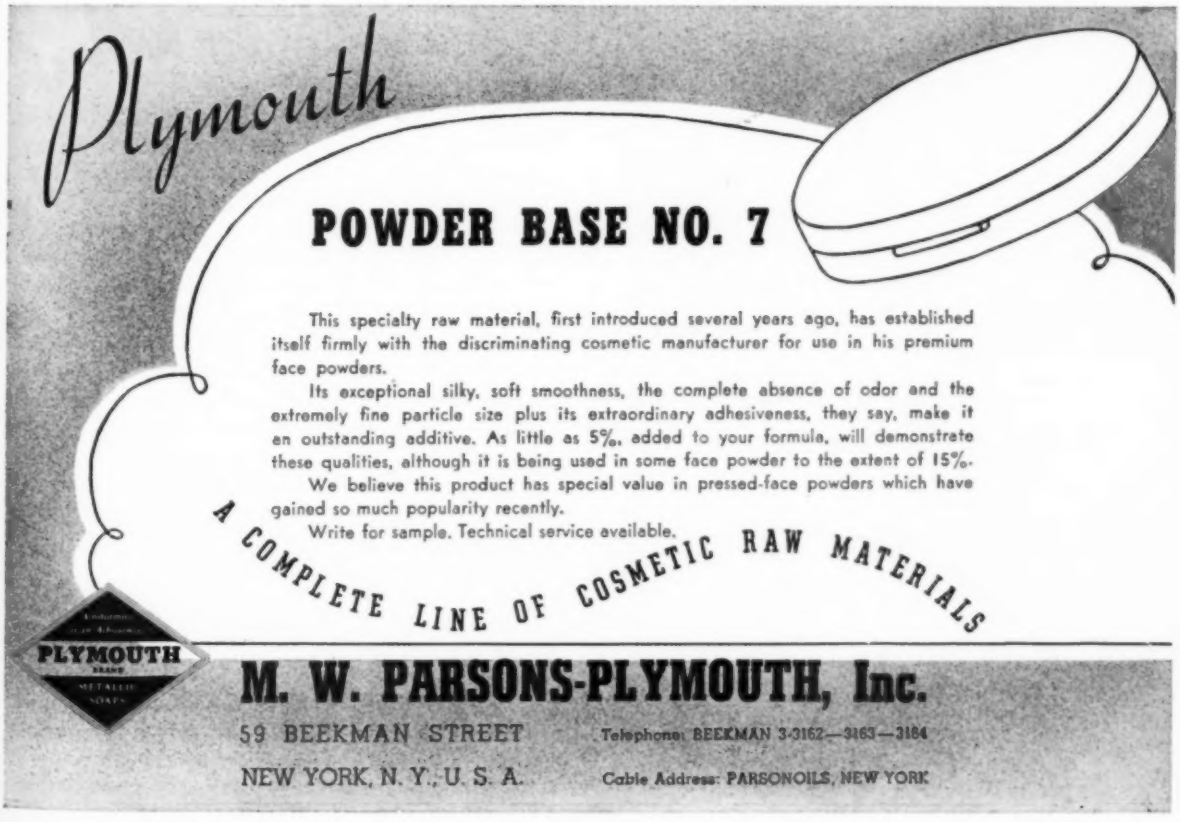
Apart from reserpine, the next pure alkaloid of interest is one variously called raunormine, canescine or deserpidine. The work on this alkaloid is still in the clinical stages with several laboratories. It has interesting prospects of action similar to reserpine, and some clinicians have commented on the lack of side effects.

Pharmacological studies on such alkaloids as raunormine and raunescine (from *R. canescens*) are under way, but the clinical applications are not yet apparent.

V. Where Do We Go from Here?

The four known actions of the commonly used *Rauwolfia* preparations are:

1. To lower blood pressure—this is the main use of whole *R. serpentina.*
2. To tranquilize—for this action reserpine has been the choice.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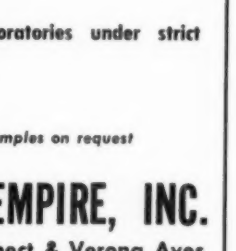

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3. To slow the heart rate—again reserpine.
4. To tranquilize and to have mild sedative action—for this the selected groups of alkaloids or whole, standardized *R. serpintina* root and reserpine are all used.

From the standpoint of uniqueness, perhaps the most important effects are those having to do with mental disorders.

The *Rauwolfia* preparations, together with such synthetic organic chemicals as chlorpromazine and meprobamate, have been hailed as one of the greatest contributions of the century to medicine. These are the first drugs to be used in the chemotherapy of mental disease, and as such, they have been directly responsible for wonderful progress.

The next stride forward is difficult to foresee. The writer hesitates to go into the pertinent aspects of organic chemistry, but doubtless there will be other chemicals beyond chlorpromazine and meprobamate. But the author and his associates have explored for *Rauwolfias* and related plants in tropical lands and it is equally certain that the plant kingdom still hides much to be discovered.

The *Rauwolfias* are tropical plants. Relatively much has been learned about them in a little over five years. But in this same family of plants, the *Apocynaceae*, there are at least another 100 species about which little is known—except their names. And there are probably as many more species of *Apocynaceae* as yet unnamed. In that reservoir there must be something more to be found of value to medicine.

THE TRANQUILIZING DRUGS

(*Continued from page 473*)

Insulin, and especially electric shock treatment, introduced less than twenty years ago, marked a very important step in the treatment of major psychosis. In depressions it is still the best we have and it keeps people from committing suicide and it limits the depressive spells to a few weeks.

It is, however, less effective in psychoses where anxiety is in the forefront of symptoms. Where agitation is extreme the patient has to be hospitalized. There are also some people whose physical condition is so poor, that shock treatments are contraindicated. Since the effect, even when good, is cumulative, for quite a while supervision and management of the anxious psychotic remains a problem. Even when the effect is eventually good enough, you cannot offer a continuous, self-administered maintenance shock therapy to assure the fixity of improvement.

This state of affairs was then the background in which the tranquilizing agents came into usage. And let me state emphatically that while a considerable measure of success has been achieved with the tranquilizing agents now at hand, the hope of medicine is predicated on the possibility that improved versions of these drugs will be soon in our reach.

Besides anxiety, whether part of a neurosis or a

psychosis, and its physical expression called nervous tension, there are a number of conditions and symptoms where anxiety is a contributing factor, attached to all kinds of diseases, including organic ones. This means that besides anxiety plain and simple, there are such conditions as coronary heart disease, hypertension, peptic ulcer, asthma, neurodermatitis, itching, nausea, and the well known symptom of most illnesses, namely, pain, which all have anxiety as a component. The area of indication for tranquilization by drugs, therefore, encompasses practically the whole medical field. It is, therefore, not surprising that patients who need pain killers, narcotic or non-narcotic, habit forming or non-habit forming drugs, now need considerably less of these if the anxiety producing element of pain is successfully eliminated or decreased by the non-habit forming tranquilizing agents.

It is also easy to see how drugs which, either during wakefulness or sleep, are able to hold down nervous tension most of the day are useful in reducing the bodily manifestations of chronic anxiety attached to the so-called psychosomatic disease. Tranquilizing agents, therefore, became aids in therapy not only in psychiatric practice but in every branch of medicine. Just take a common symptom such as insomnia. Patients who needed two sleeping pills to secure a good night's rest were able to reduce their needs to one or none if taken in conjunction with tranquilizers which prepare an individual to the sleep producing effect of barbiturates which it reinforces.

If we can talk about a revolutionary advance in the handling of patients by the use of these new drugs, please consider the change that took place in the handling of the mentally ill in state hospitals. In many large institutions the necessity to use electric shock and insulin treatment has been reduced by fifty per cent since tranquilizers have been able to decrease the marked anguish, the hostility and the disturbed reaction that beset the thousands of psychotics who used to languish in the violent wards of our mental institutions. Consider the gain derived from the reduction of stupefying sedatives, body restraints and, last but not least, in supervisory personnel, of which no hospital ever had enough. Consider the gain when the physically debilitated psychotic who could not have tolerated shock treatment, now can be handled successfully by the use of a couple of pills a day; deteriorated patients, whether in a senile group or young, have been promoted forward from the deteriorated wards toward those sections of the state hospital where they can look after themselves and besides becoming calm enough to go out of the building to participate in physical activities they are now calm enough to sit and participate in occupational therapy or group therapy. Many of them became even accessible to psychotherapy. Treatment by drugs in this category of mental patients may have to be given for two months, a year or all the time, but the saving is still enormous in terms of suffering. Depending on

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how old the mental illness, or what its nature, from thirty to sixty per cent of these drug treated patients could be discharged, though most of them still have to take the pills and check with the clinic or the psychiatric social worker. Some, caught early in the illness, went into remission after a month or two, but what is even more striking, quieted down in the first day or week after admission.

These drugs posed interesting problems in state hospital management. Since the disturbed patients quiet down, the hostility of those who suffer from delusions of persecution yields to friendliness, even to gratefulness, and a new segment of state hospital population becomes available to psychotherapy. This in turn makes it a necessity to spend more money on hiring more doctors in order to treat these patients psychologically and to prepare them for outside existence.

But once again—let us emphasize more than anything else—the discharge rate went up and as we learned to give more and more of these drugs, the reclamation for useful life of the mentally ill is going up and up.

One of the outstanding successes was achieved in the elderly senile patients who shortened their lives by their agitation, refusal to care for themselves, and refusal to eat. Many of these can now be kept home, they can even help with the work around the house.

As I am carried away and praise these drugs, the dangers of their indiscriminate use comes into my mind. I know neurotics receiving psychotherapy who, when these drugs reduced their anxiety, quit their psychotherapy. But I am thinking of the danger of giving these drugs to seriously depressed patients, who may get worse and try suicide, while electric treatment given *instead* could clear up their depression. I am thinking of the doctors who give too little and then, in their disappointment, conclude that the drug is no good.

It may be that with better drugs now in the making and with more experience, most patients will be cared for at home. Nothing would erase the stigma of mental illness more than the abolition of commitment to mental hospitals, allowing the mentally ill, just as other ill persons, to stay within their family circle.

There are those who hold the opinion that these tranquilizing drugs, because of their spectacular effect on the serious mentally ill, would brand as insane anyone who uses them. I hope what I have said so far dispelled this prejudice which has no foundation in fact. *Tranquilizing agents are good for everyone who needs them*, though perhaps it is true that the more nearly normal a person is, that is to say the less such a person needs it, the less dramatic its effect. They do little for pure depressions and for the so-called comfortable neurotic and psychotic. They do not change the thought content of the compulsive-obsessive. And we still do not know when to stop giving the drug in

every case. Not enough time has elapsed to tell exactly how many of the improved cases will relapse.

As we pass in review the field of indication of these drugs, let us not forget the alcoholics, many of whom at present reaches for a tranquilizing agent when he gets the well-known jittery feeling that in the past used to direct him toward the bar and bottle.

Now a word about the kind of tranquilizers at our disposal at present, their best use and abuse, and the liability of side effect.

One of these agents, as you all know, was known for centuries in India and I am referring to the extracts of the plant Rauwolfia serpentina or Indian snakeroot. Purified elements of the rauwolfia extracts, the most valuable element of which is called reserpine, enjoy the largest usage, administered in amounts that may enormously vary from one person to another and from one condition to another. Therefore, no one should attempt to start using these drugs without a thorough-going physical examination allowing the physician to *tailor* the dosage to the individual's needs and under close supervision for at least as long as the doctor is able to convince himself that the dose is safe and effective.

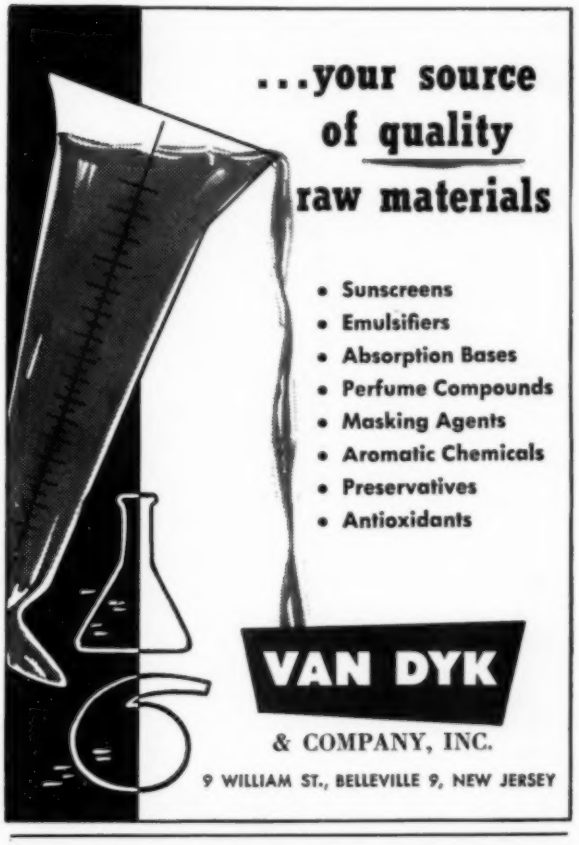
More is known about the chemical mode of action of reserpine than the other tranquilizers. The chemical formula (an indole ethylamine) resembles that of a vasoconstrictor principle found in blood, called serotonine. Reserpine and serotonine metabolize into the same end products. Serotonine is present to the extent of one-half microgram per gram in the brain—where it is mostly concentrated in the hypothalamus and brain stem. Injection of reserpine liberates serotonone from the tissues, and in the brain more than in any other organ, the freed serotonine is believed to be responsible for tranquilizing.

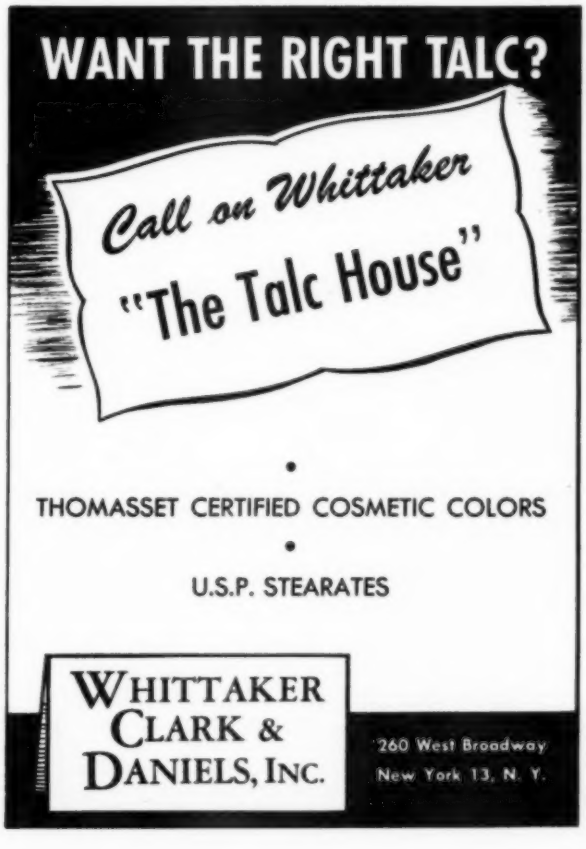
Serotonine is formed in the body out of an amino acid: tryptophane. Reserpine produces a change which results in high intracellular and low extracellular concentration of serotonine. It destroys therefore the *binding site*, the point where serotonine is bound to the cell.

Even though reserpine is quickly metabolized and out of the system, its serotonine mobilizing effect persists for eight hours. It may take a week before the daily reserpine destroys enough serotonine binding sites so that enough serotonine is freed into the circulation to start tranquilizing. It should be stated, however, that the reserpine-serotonine combine does more than tranquilize. It potentiates hypnotics, it lowers blood pressure and temperature and it has a less defined gastrointestinal action.

It is, in other words, a drug which affects chiefly emotion and its physiological expression. It is not surprising then, that reserpine overdosage sometimes produces a Parkinsonian syndrome—for it is in this condition that we see the most extreme examples of frozen emotional and motor expression.

This drug reduces blood pressure to a variable ex-





tent in many and therefore it is best taken either when going to sleep or when arising before getting out of bed. Where Parkinson's syndrome appears interruption of the medication causes it to disappear or else it responds successfully to the usual drugs given for Parkinsonian tremor.

Chlorpromazine, the other drug, is an anti-histaminic of a sort which was discovered in France and it was found that it acts as a sedative in the brain center of the autonomous nervous system thereby reducing the overactivity of the various organs in the body which this nervous system controls. As a result, anxiety, which after all is experienced through these organs, if deprived of its means of expression, disappears as a *feeling* even though anxious *thoughts* may still be present. Chlorpromazine produces physiological and psychological changes, leaving consciousness and ego functions intact. Its action on subcortical functional centers decreases *conative intensity* and kinetic energy and facilitates a harmonization of disturbed personalities. Some believe that it suppresses excitation, in other words, it acts like a temporary chemical lobotomy. As is the case with Reserpine, its maximal point of action then is in the general area of the viscero-psychic functional system, the most primitive part of the brain. It too may lead then to a Parkinsonian syndrome and overdosage can be seen in the form of loss of drive, apathy and emotional lameness.

This drug was quickly converted to psychiatric use in any mental illness, major or minor, which is associated with agitation, and anxiety is beneficially effected by it. Because of its potentiating effect on barbiturates and narcotics, chlorpromazine more than any other drug contributed to the reduction of the effective dosage needed by the patent for proper relief. The amount varies from 75 to 4,000 mg. per day, but here again side effects have to be looked for, recognized and dealt with. Apart from the common complaint of dryness in the mouth and stuffiness in the nose, the moderate degree of reduction of blood pressure, skin rash and constipation, this drug in less than two per cent of the cases, causes a form of obstructive jaundice which disappears after interruption of medication. Very rarely it has a destructive effect on the blood forming organs, consequently, particularly during the first few weeks, close watching of the blood count and the blood picture in general is a necessity. When agranulocytosis appears, the drug has to be discontinued at once. Also reported are such side effects as were described about the rauwolfia. One should, however, keep in mind that though rarely—a variety of side effects were noted, which may appear like a new illness, like ringing in the ear, seizures, abdominal cramps, swelling of the face and ankles—which all disappear when the medication is interrupted or decreased. It has been found that a combination of the rauwolfia derivatives and chlorpromazine often works better than either alone, and it may be possible to obviate such side effect as may be caused by the excessive dosage of either.

The most spectacular side effect is jaundice which in the overall statistical surveys occurred in a little over one per cent. Most of the cases have taken a lot and for a long time, though occasionally it occurred after a few weeks of taking a few tablets a day. In some state hospitals, chlorpromazine was not even interrupted when jaundice occurred and yet, it cleared up after four to six weeks.

A third member of the tranquilizing drugs, most recently introduced, is called meprobamate. Meprobamate (Miltown, Equanil) is said to act by relaxing muscle tension through intervention at the interneuronal level. This means, that as impulses are streaming down from the brain to the motor cells in the spinal cord—much of this excitation is blocked at the cord level—so that tension—in the form of tight muscles and painful spasm, is no longer felt.

Because of its predominantly peripheral effect—it does not seem to lend itself to quieting the extreme storms of excitation that we see in psychotic behavior, especially in the manic state. On the other hand, it is the best, safest and simplest drug for the ordinary tension that beset so many otherwise healthy people, who have difficulty in getting "unwound." This drug may turn out to be the major answer to alcohol and barbiturates as used by the average "nervous" person.

All these medications mark a substantial advance in our attack on emotional and mental illness, whether it is implanted upon an organic disease or not. Confronted with the success of these drugs, research centers and the drug industry are hard at work to bring out similar drugs which would be of even more benefit, which are safer and more applicable to the maximum number of people.

MODERN CLINICAL RESEARCH

(Continued from page 471)

the patients receiving the drug in comparison to similar complaints made when a placebo or the standard drug is given. Using these observations it is possible to arrive at a rough approximation of the clinical "toxicity" of the agent (in the doses used) and by employing this information and the potency data to arrive at what is called a "diuretic index" which can be interpreted as a comparative value of clinical utility.

This is, I think, typical of a human bioassay. A single measurement which is considered to be valid for indicating potency of a drug is made on patients particularly selected to show alterations in that measurement in response to drugs having the type of activity being studied. More than one dose level is employed so that a "dose response curve" is obtained. This curve is compared to a similar one obtained with a standard and with an inactive placebo. In the instance cited, it is believed that this is an accurate reflection of the effect of diuretic agents on renal

function in patients with edema. It is obvious, however, that if the measurement selected does not reflect the useful activity of the new drug being tested, the bioassay will have no value whatsoever.

Referring again to our study of new diuretic agents, we submitted first one and then the four most promising of our forty-one experimental diuretic materials for evaluation by this human bioassay technic. Within a period of *three months* it was reported that one of these agents was "best" and that a certain dose was the equivalent under the described conditions to a certain quantity of a standard diuretic. It was the same drug selected by the eight year "clinical trial" method. It is clear that a properly designed experiment in human pharmacology can remarkably shorten the time necessary to determine whether a new drug is of value.

Even so, as mentioned above, a human bioassay by no means gives all the information on a new drug which is required to describe the utility of that drug in general practice. With the exception of subjective complaints of "side effects" it gives no information whatsoever on other actions of the drug, it gives little insight into the mechanism by which its therapeutic effect is produced, it does not take into account the response of individual patients with varying degrees of severity of the disease, it does not measure the effect of concomitant therapy or variations in that ancillary therapy, it carefully eliminates the effect of your own personality upon the response of your patients, it does not include in its "potency" value patients who are refractory to any drug with this type of activity, it gives very little information concerning the response of patients who may be particularly susceptible to the untoward effects of the drug, it does not give information regarding the long continued use of the drug, it does not take into consideration the natural history and progress of the disease being treated.

Why then do it? Within a short time it will discard those agents which are not effective or are no better than agents already available. It will also certainly materially shorten the period before the exact status of a new drug in clinical practice is determined since with this prior information it is possible to precisely define the type of further experiment which is required to determine the actual practicality of the new agent.

Many of these further tests can and should be carried out under very strict experimental conditions where as many factors as possible are controlled, and where the double blind technic is employed. On the other hand, many of these questions can only be answered by general use without precise regard to "control." In fact it is agreed that it is desirable to have experience in the routine (as opposed to "experimental") use of the agent, by a cross-section of the profession in the actual treatment of disease, prior to the introduction of that drug. It is only in

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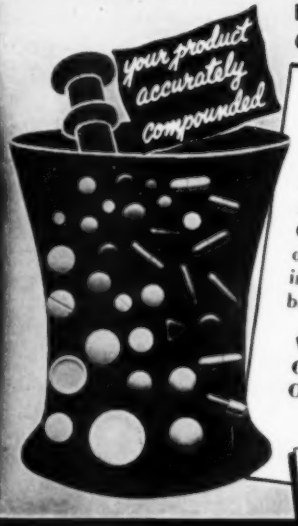

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this way that one can obtain sufficient numbers to insure that the "average" figures which are given you regarding dosage, expected response, untoward effects, and the like have some relation to reality.

The very elaborate experiments in human pharmcology or drug evaluation which are frequently employed are elaborate largely to control as closely as possible the many variables which may affect an individual's response to a given therapeutic procedure. I do not need to elaborate on the multiplicity of those variables; I do wish to emphasize that to my knowledge no experiment has ever been so successfully designed that *all* those variables have been controlled. On the other hand, I have been very much impressed by the fact that a good clinician, a "family doctor" if you will, who knows his patient thoroughly with all that that implies, who understands the natural history of the disease which the patient presents, and who understands the variables which may affect the response of that patient to a therapeutic agent can do a magnificent job in weighing those variables and consequently accurately determine in a very few patients the effectiveness of the drug which he has used. Clinical judgment applied to new drug testing can of course be very wrong indeed; and in all instances must be put to rigid test to determine its validity. Nevertheless, we value those opinions highly.

Finally, I believe that any physician's use of a new drug, or for that matter any therapeutic procedure, new or old, should be considered as a "clinical trial." Certainly all physicians form their own opinions of the worth of any procedures which employed and their own use of that procedure is of course the evaluation on which the new drug will stand or fall. I do sincerely believe that in judgment of that agent it is necessary to remember the principles of bioassay, some of which have been outlined. It is necessary to remember the size and character of the population sample being examined. It is necessary to weigh the accuracy of the methods used to determine response and the variability of those measurements from patient to patient, and from time to time in the same patient. It is necessary to consider the fact that "personality effects" are real and that "placebo effects" do occur.

Finally, remember that first results often require further confirmation and only on the basis of this should final judgment be made.

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SUNTAN PREPARATIONS

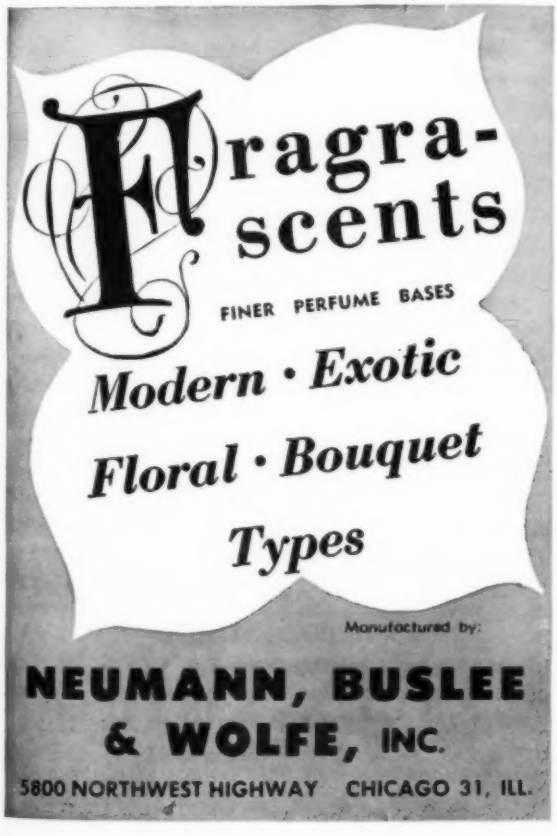
(Continued from page 463)

Another approach would be by the use of emulsifiers which after application of the film, would be removed from the film through evaporation or through absorption by the skin. The well-known ammonium soaps are an example of the first and in many cases

some quaternary ammonium compounds may be removed through absorption to the skin proteins thereby leaving a substantially water repellent film. A combination of these ideas with a silicone incorporation would probably be even more effective.

The advantages of the emulsions lie not only in the greater scope given the formulation in the choice of materials one could use, but in the more pleasant application as far as the user is concerned. I am convinced that the greatest appeal of the emulsion lies in the pleasantness of its use rather than in the technical advantages it could offer. I am also certain that the consumer would rather use an emulsion than a clear liquid, whether it is alcoholic or oil—other things being equal.

One of the newer vehicles which we are all conscious of is the propellent bomb. This newer product, though it has not yet had much effect on suntan preparations, would be ideally suited as a method of application. The vehicle could be the propellent and an alcoholic solution of the sunscreen or if preferred, the propellent and fixed oil. In any case, the ratio of the propellent to the concentrate could be fixed to enable the consumer to spray a film of adequate sunscreen concentration on the skin uniformly and with a minimum of trouble. In addition, there need not be any substances incorporated which could conceivably cause a mechanical failure to take place because of corrosion. The propellent mixture may be fixed so that the spray is of the right droplet size and of optimum pressure for application over a relatively large surface. The only



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flaw which may become immediately apparent is that the user must be cautioned about keeping the spray from the eyes, and should be warned to apply the preparation by first spraying on the palm of the hand and then transferring the film to the face. Application by means of the bomb, seems easier than pouring from a bottle and then transferring the film to the face. Application by means of the bomb, seems easier than pouring from a bottle and then transferring to the arms and legs. The container also is better adapted to the beach and rough usage than is the usual bottle.

There have recently appeared on the market, and indeed patents have already been issued for their use in sunscreening preparations, a class of materials known as optical bleaches. These compounds, some of which are substantive to proteins, reflect ultraviolet light as visible light. The fact that some of them may be substantive to the skin would make them ideal agents as sunscreens! It would be interesting to watch this development.

THE EUROPEAN FREEZE AND PERFUME OILS

(Continued from page 467)

ing the twentieth to thirtieth years. A ten year tree produces about six kg. of flowers yearly, an older tree up to 20 kg., 5 to 10 kg. being the average in Southern France where the trees are smaller than in North Africa. The bitter orange tree has a long life span, eighty to 100 years not being exceptional. The farmers consider the groves, usually inherited from their ancestors, as a valuable family possession, which they are loath to abandon even when flower prices fall to unprofitable levels. For this reason the orchards of Southern France have withstood many severe economic crises, except for the very old groves which are left to die without being renewed.

In addition to the oils obtained from the bitter orange tree, other oils have also been seriously affected. The mimosa trees have all been frozen over, so that there will be no more fresh flowers this season. Only the flowers brought in before the freeze can be processed to obtain oil. The situation looks very dark so far as future supplies of mimosa oil are concerned.

The violet crop, it is hoped, is not as badly off as the mimosa crop. But the leaves and flowers of the violet plants have certainly suffered to a great extent, although the damage to the leaves can not be assessed until the snows completely clear away.

The jasmin plants have also been damaged to marked extent, and supplies of this most important perfume oil are certain to be in short supply. What the future holds so far as jasmin supplies are concerned cannot be foretold until the extent of the damage is fully ascertained.

Rose plant certainly suffered from the freeze, although the extent of damage to these plants is not believed to be as extensive or severe as to jasmin and some other oils.

The Grasse geranium plants were all frozen over

It is believed that there will be little from what survives.

Also in Italy and Sicily the same conditions are said to prevail. Therefore, it is believed that flower and essential oil production from these regions can not be relied upon either. The bergamot and lemon trees are understood to have been affected. Snow also fell in the North African centers.

SUSPENSIONS

(Continued from page 469)

The addition of surfactants has a striking effect on both the viscosity of the suspension and the settling rate. Lecithin will often convert paste-like mixtures into fluid suspensions; specific dispersing agents in surprisingly small proportions will reduce viscosity and maintain the solid in suspension for prolonged periods of time. These probably act by imparting a strong and stable charge to the particles which then have a reduced tendency to form agglomerates because of electrostatic repulsion.

As a rule, suspensions incorporating the suggestions so far made with respect to the solid and the liquid phases will be more or less fluid and will not settle too rapidly. In time, however, they will settle and very often the solid will form a cake that may be very difficult to redisperse. This may be due to close packing of fine particles under the influence of gravity; it may be due to the formation of adhesive layers around particles because of chemical change. This introduces the need for another important component of suspensions, namely, synthetic and natural gums. Very obviously, the addition of one or more gums to the liquid vehicle increases the viscosity and thus tends to retard settling, and sometimes this suspending power is far greater than could be expected from a relatively small increase in viscosity. To my mind, a more important but seldom mentioned virtue of these gums is their power to reduce "packing." It may be that the individual particles are coated with a cushioning layer of the gum so that they cannot fall into a close packed arrangement; at any rate, identical suspensions with and without added gum show very different redispersion properties.

Finally, it is now possible to make suspensions which require shaking before use but in which separation and settling of the solid particles is almost completely prevented. This involves the use of inorganic suspending agents of the montmorillonite group. These complex silicates act like inorganic gums to thicken aqueous solutions and have substantial suspending and emulsifying power. Of outstanding interest in connection with suspensions, however, is the high order of thixotropy they exhibit. A small proportion of one of these substances added to a suspension containing gum and surfactant will rapidly set on standing to a gel in which no separation will occur (if formulation is correct); moderate shaking will convert the gel to completely fluid suspension for oral, topical or specialty use and the gel will quickly reform in the bottle.

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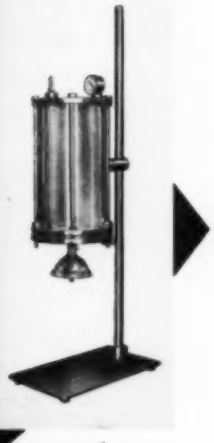

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